

Disclosures

April 4, 2016

The following planners and faculty have no financial relationships with commercial interests to disclose:

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Dita Gratzinger, MD, PhD
Ankur Sangoi, MD

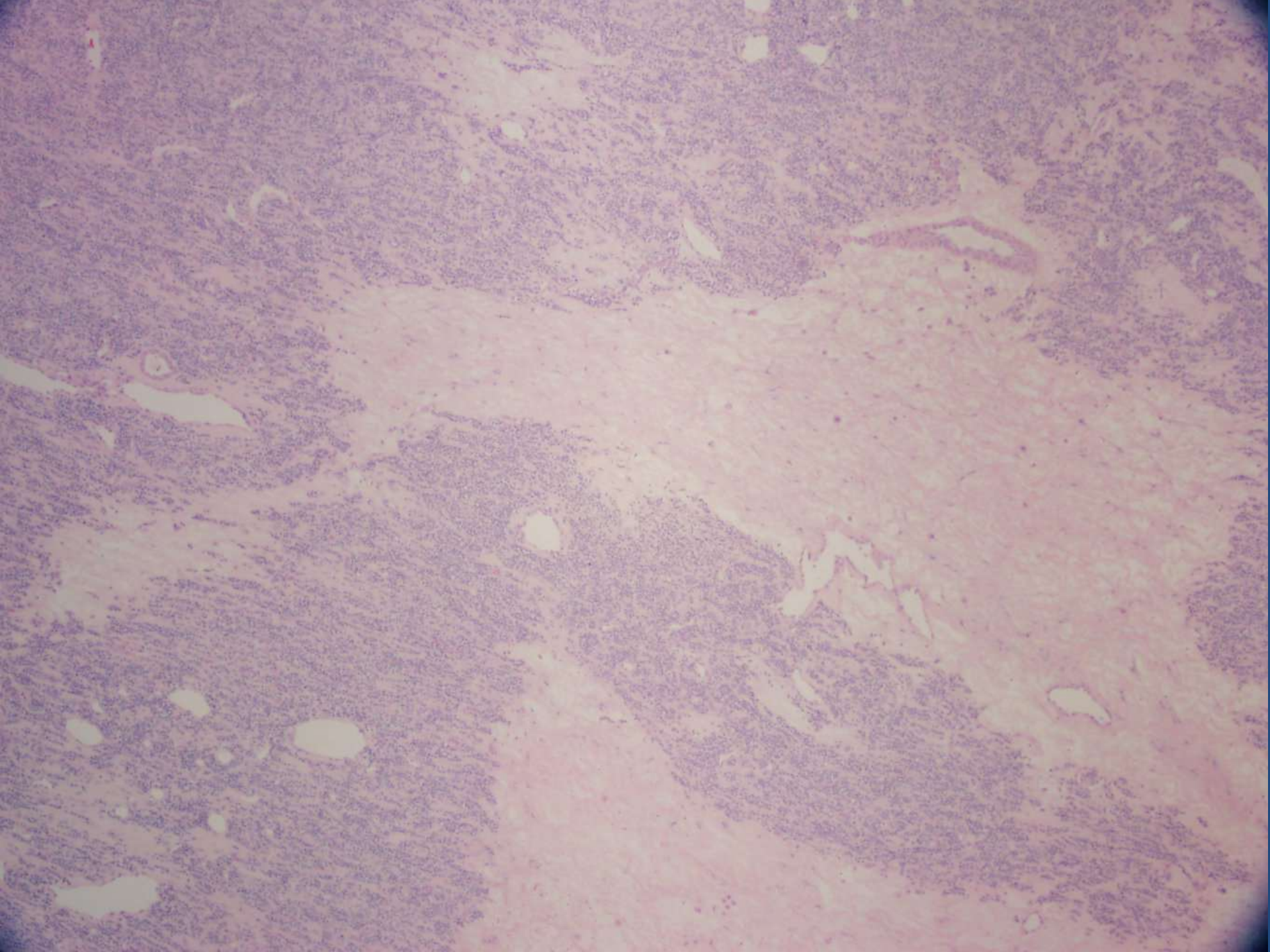
Activity Planners:

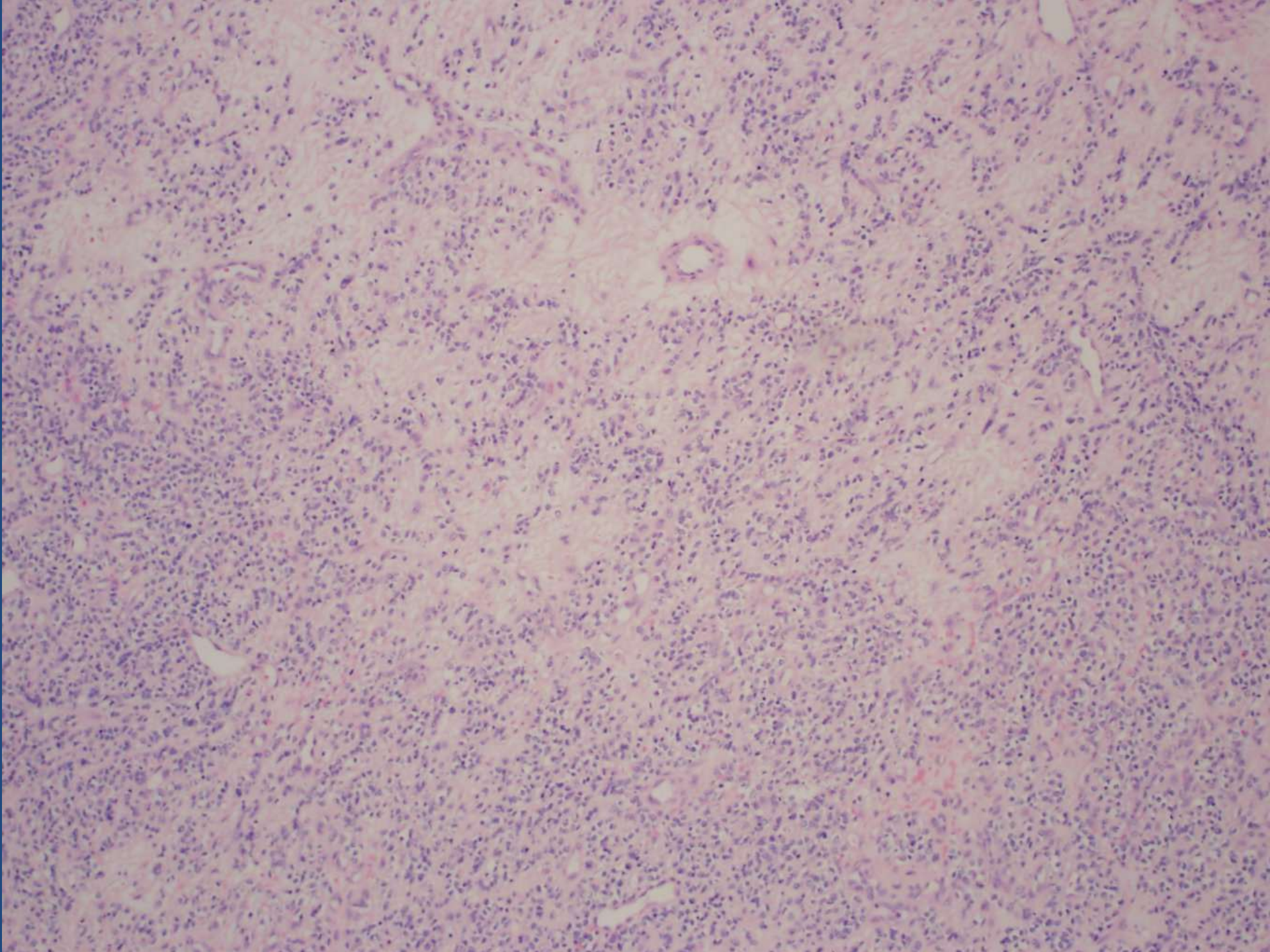
Kristin Jensen, MD
Ankur Sangoi, MD

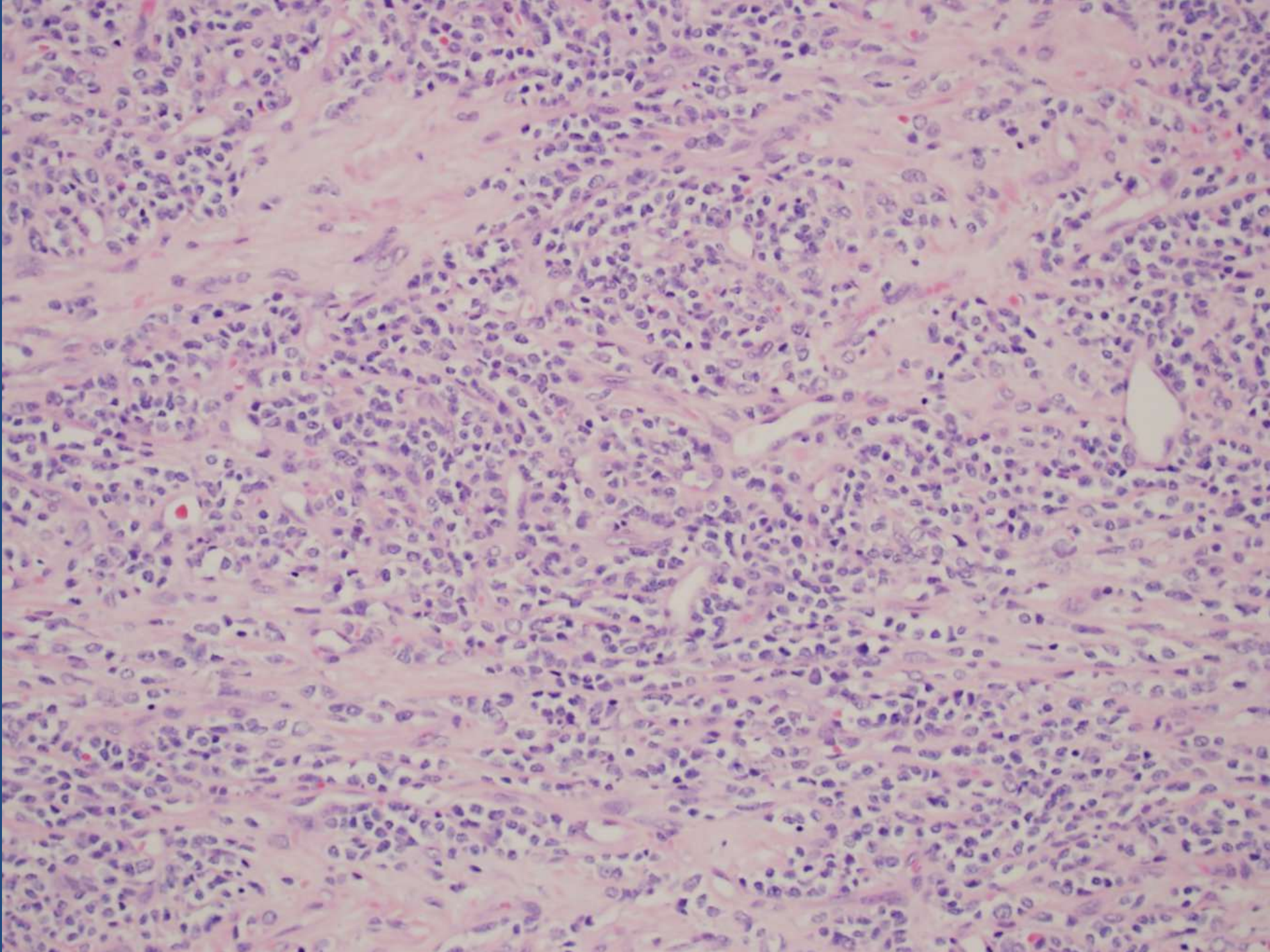
SB 6041

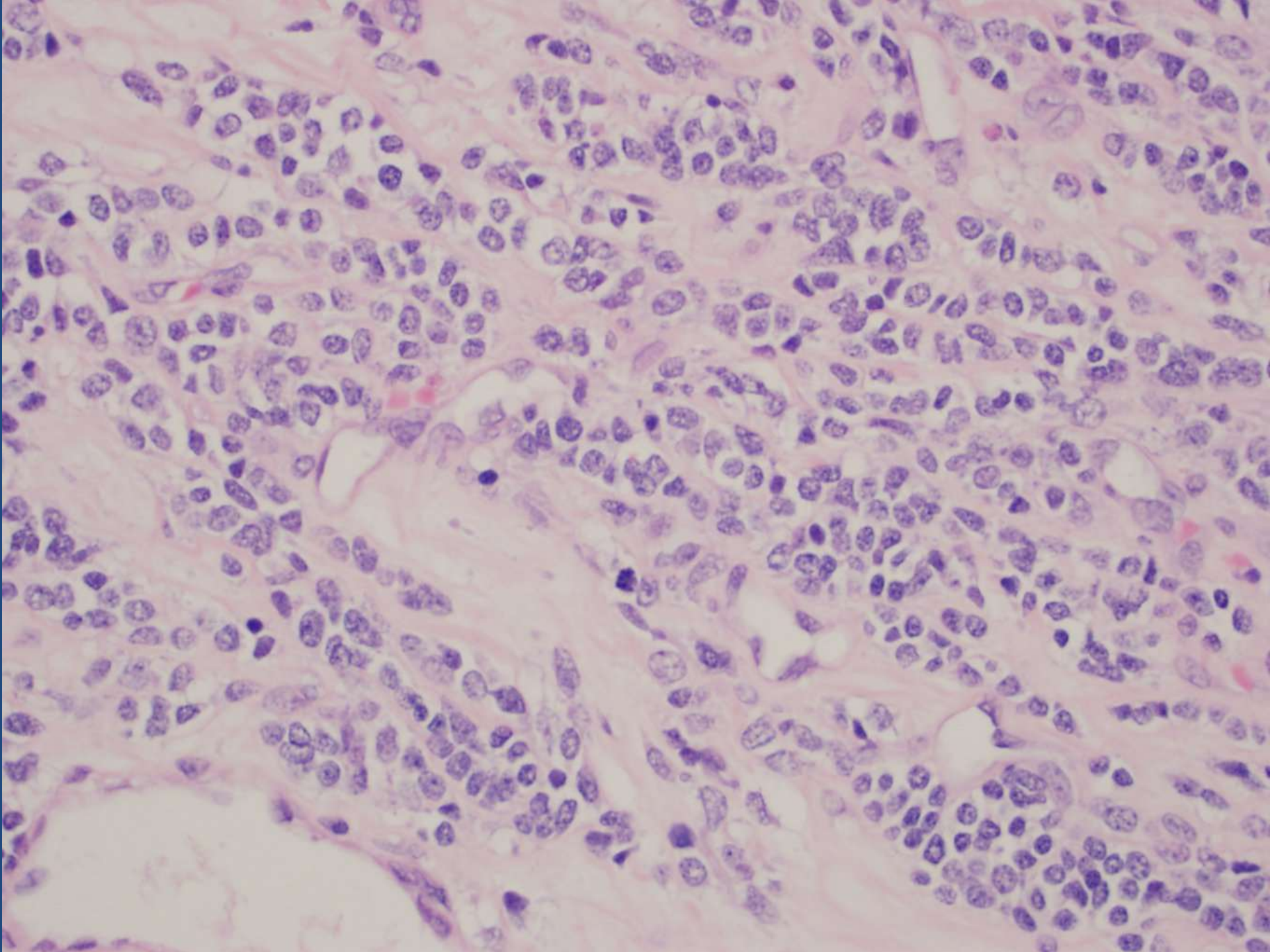
Jarish Cohen/Sanjay Kakar; UCSF

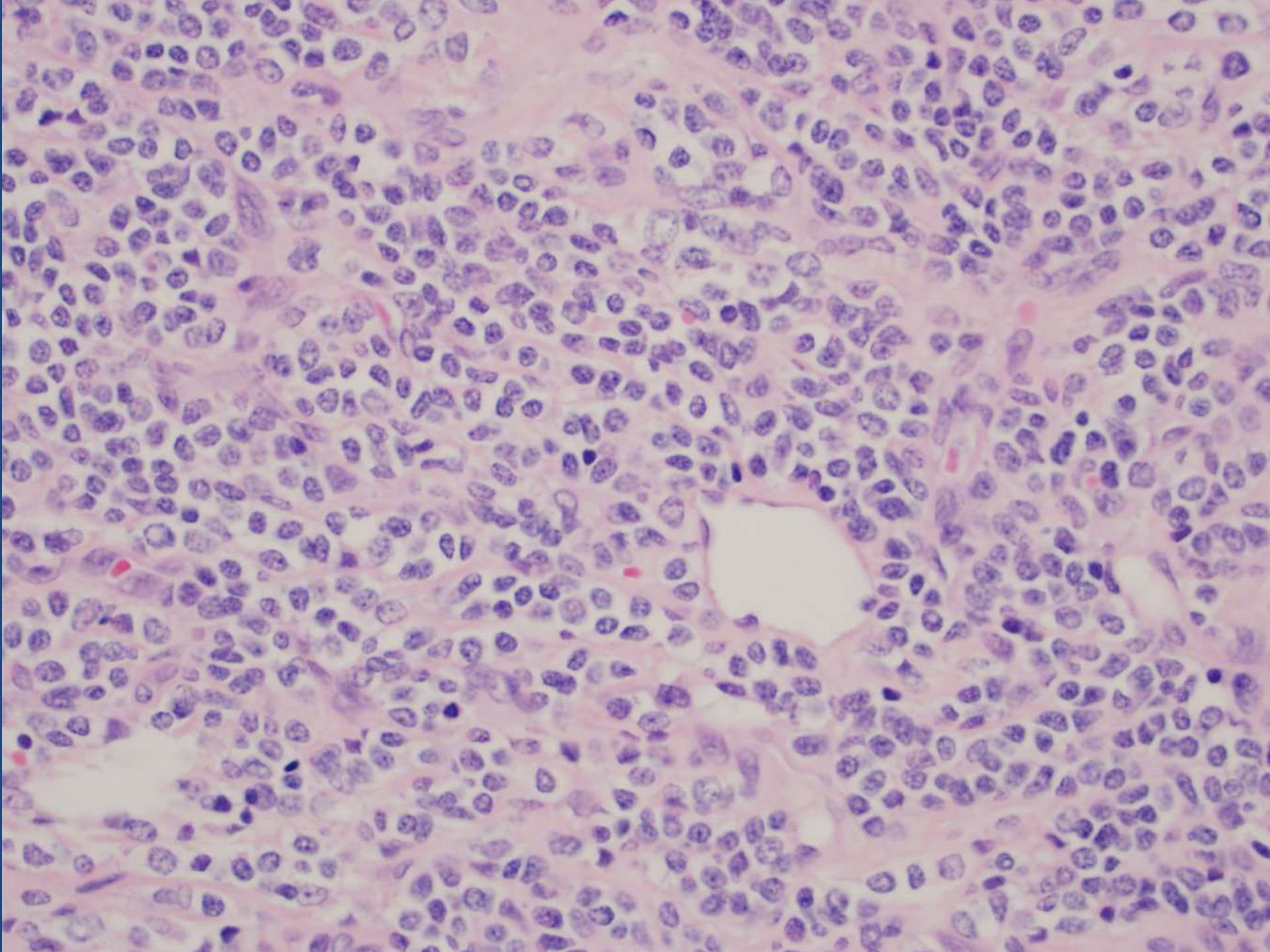
40-year-old female with a 3.9 cm partially calcified mass in the upper lobe of the right lung identified on CT imaging. Following FNA (results not available at time of review), she underwent 6 cycles of systemic chemotherapy. Follow up PET-CT showed the lung lesion to be FDG-avid, and also showed a 3.3 cm FDG-avid lesion involving the distal pancreas. She completed 4 cycles of salvage systemic chemotherapy with decreased metabolic activity in the documented lesions. She underwent distal pancreatectomy and splenectomy.

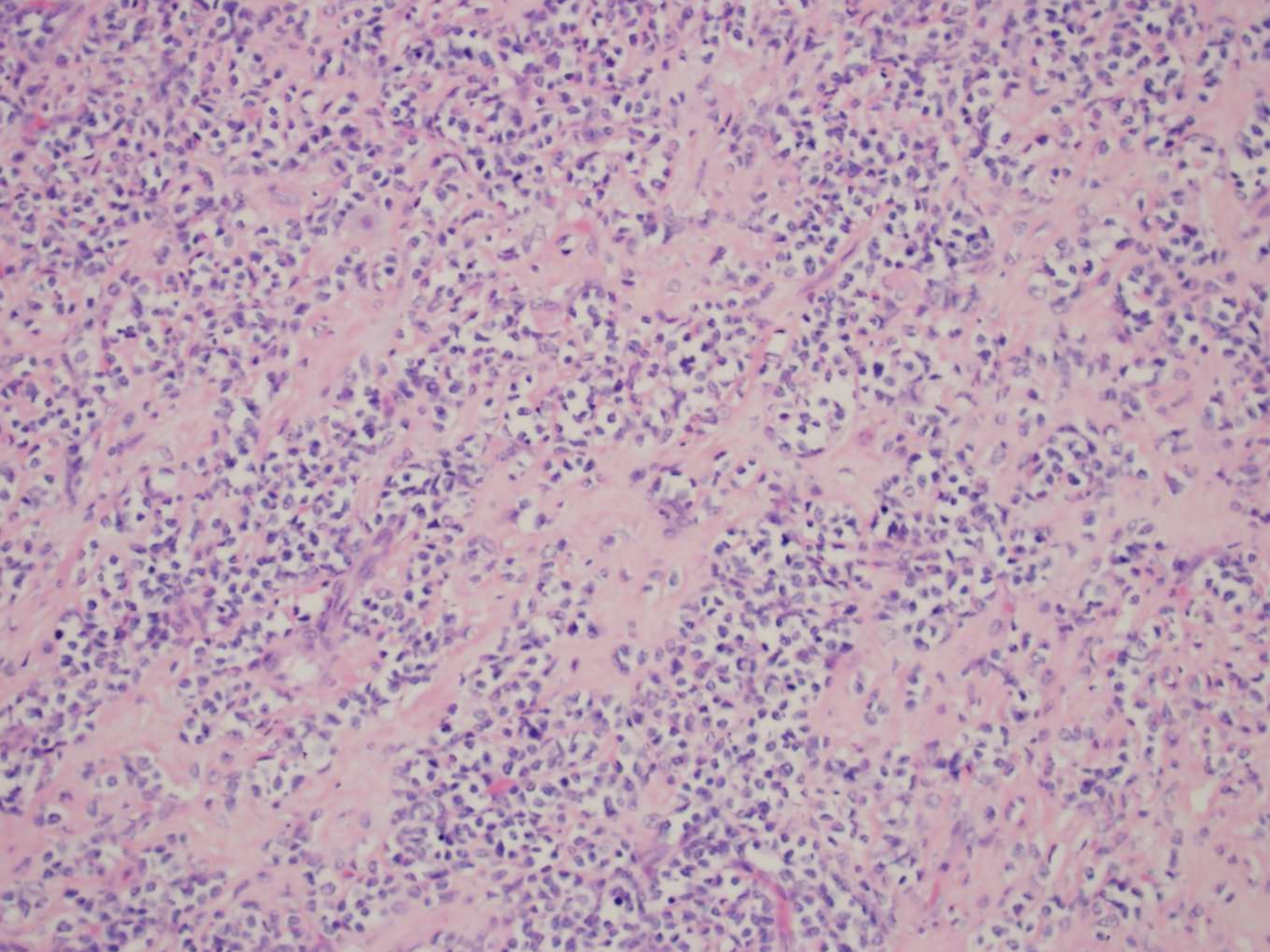


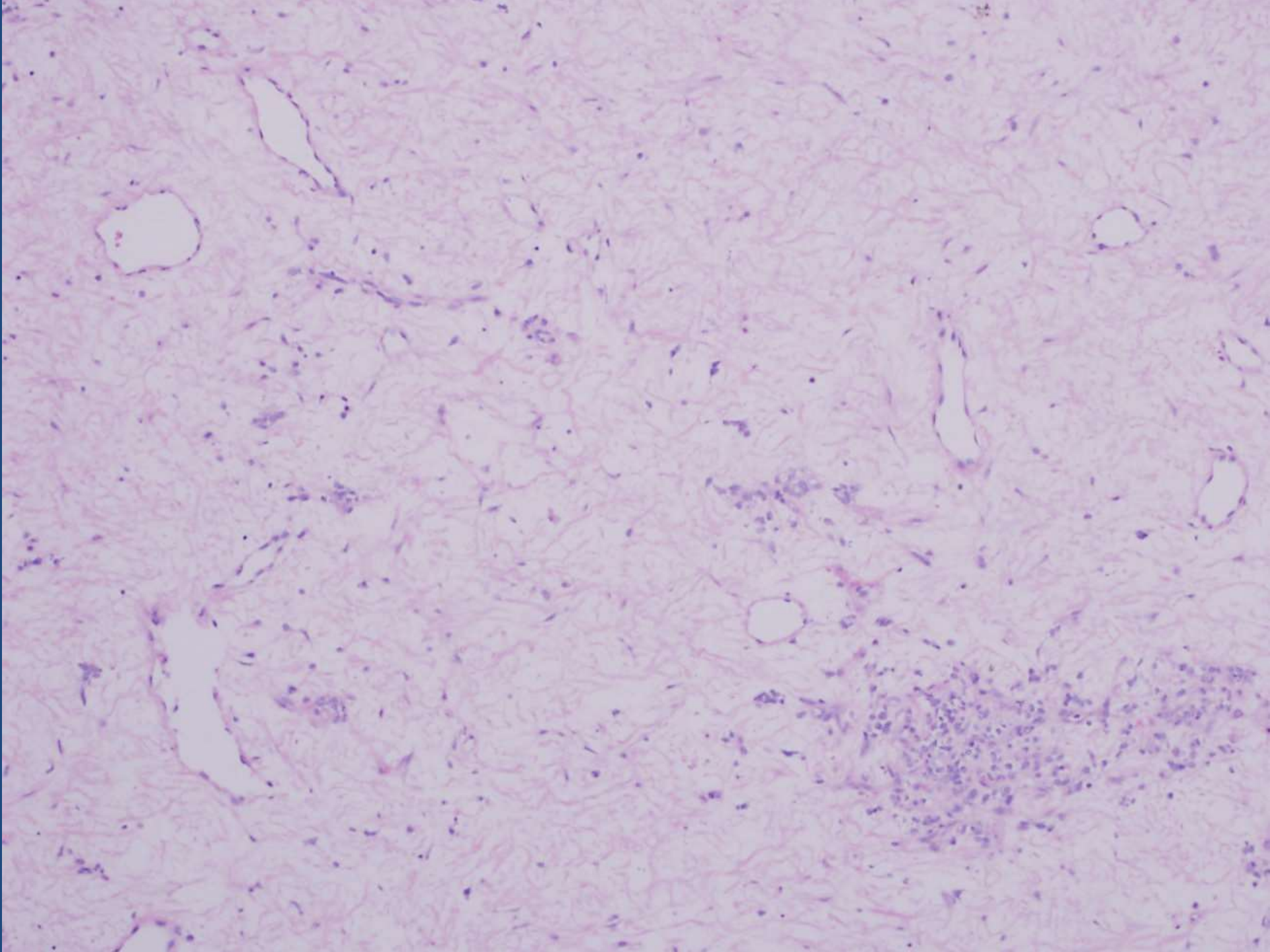


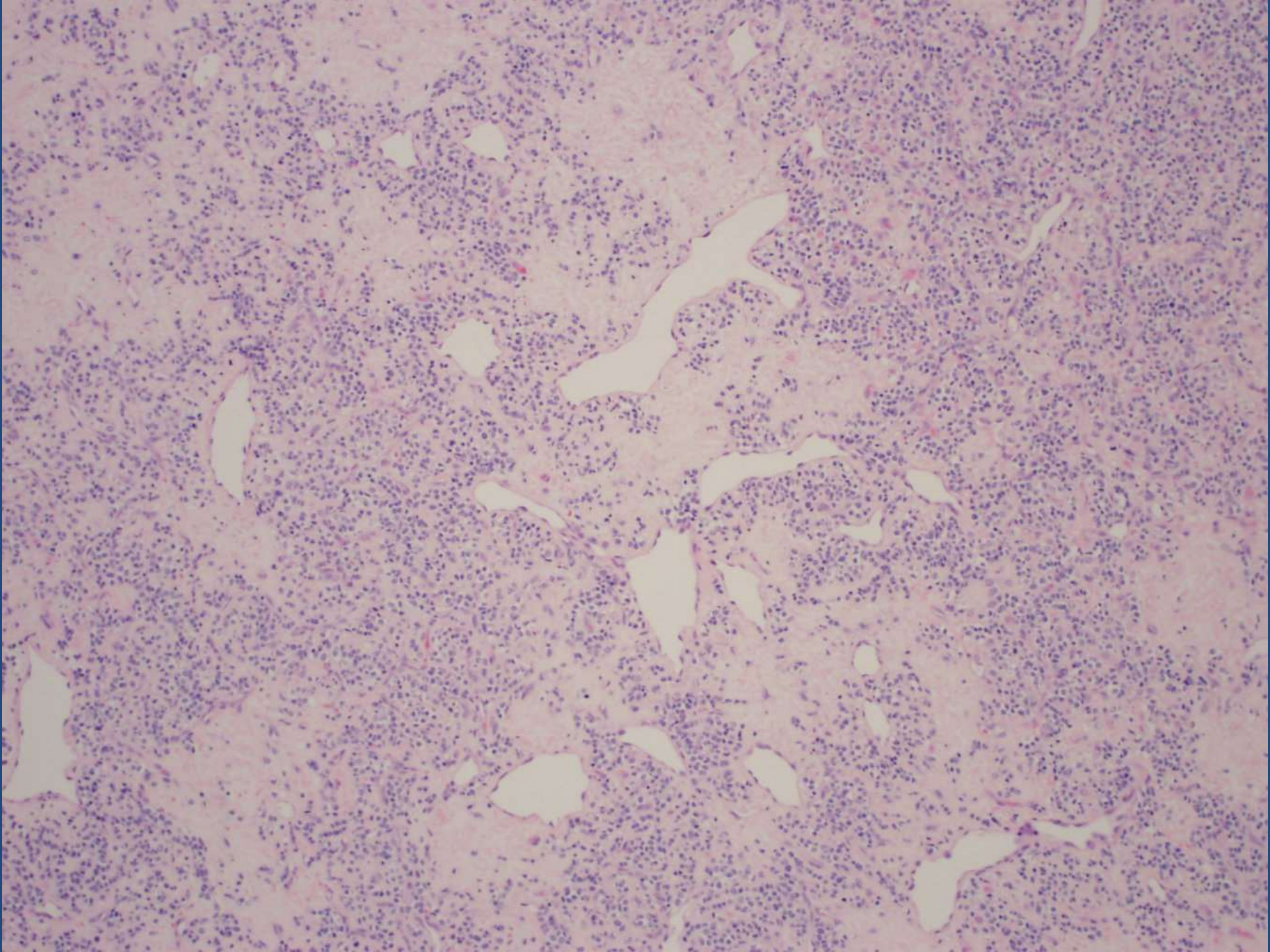


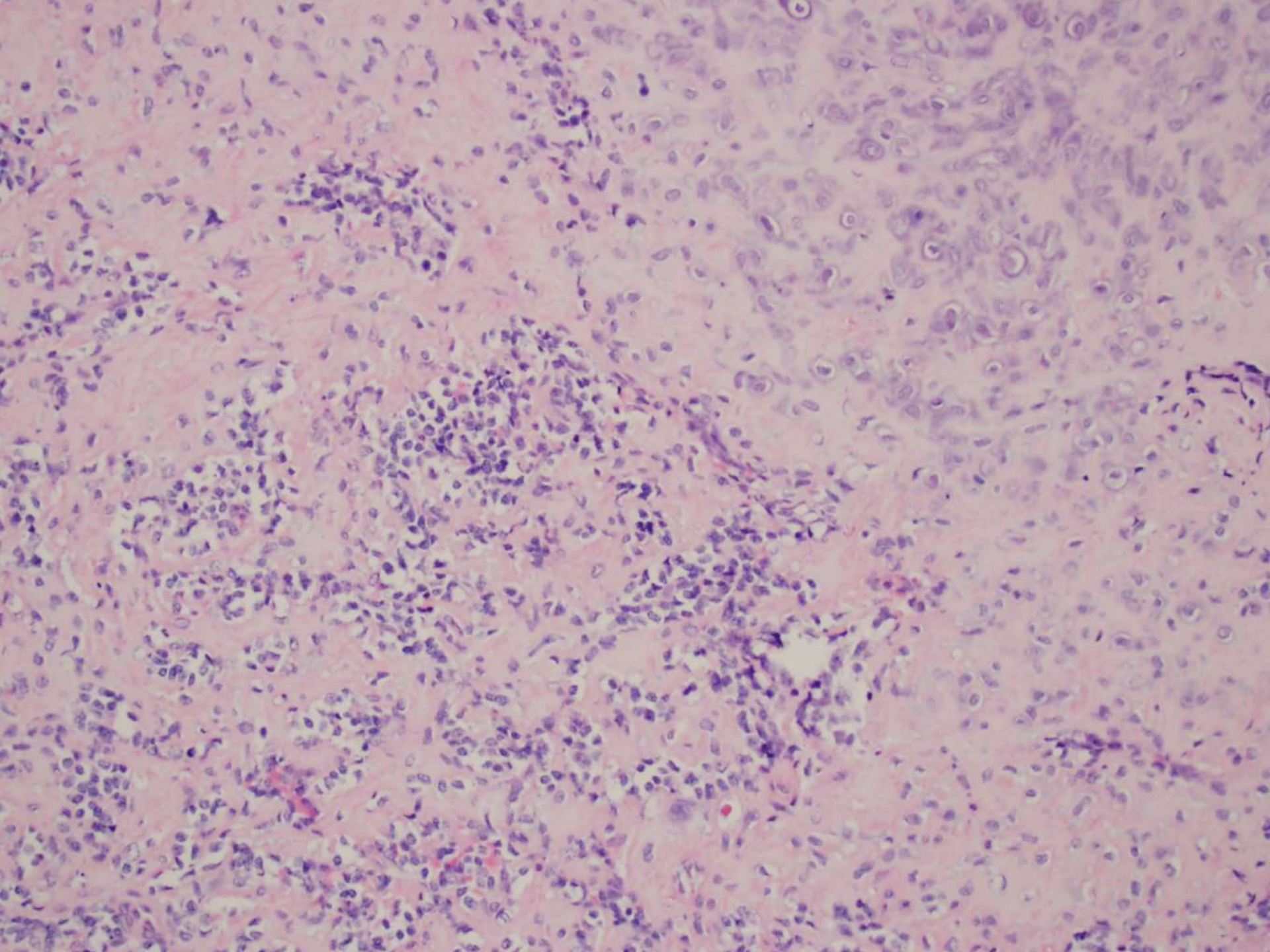


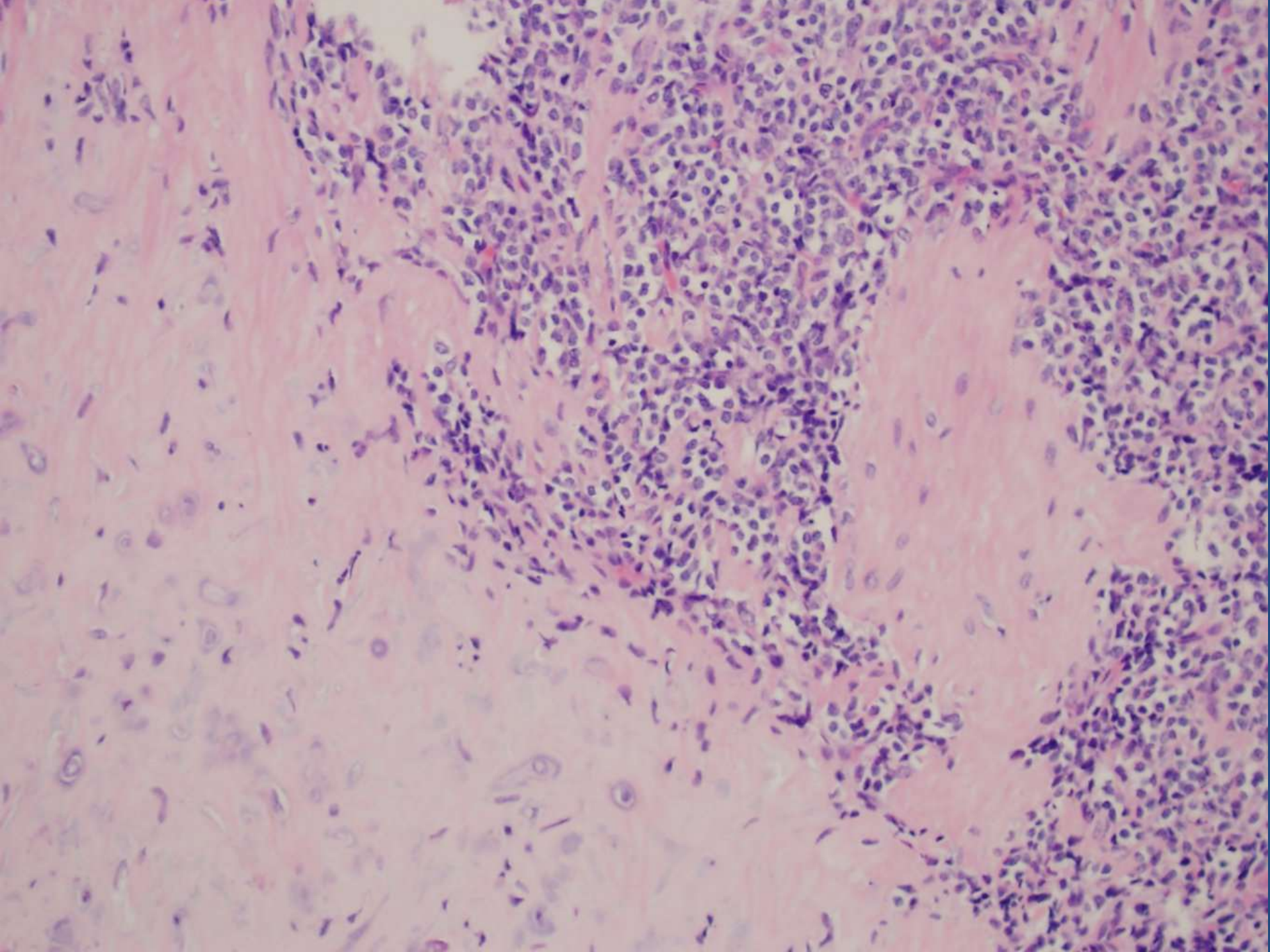




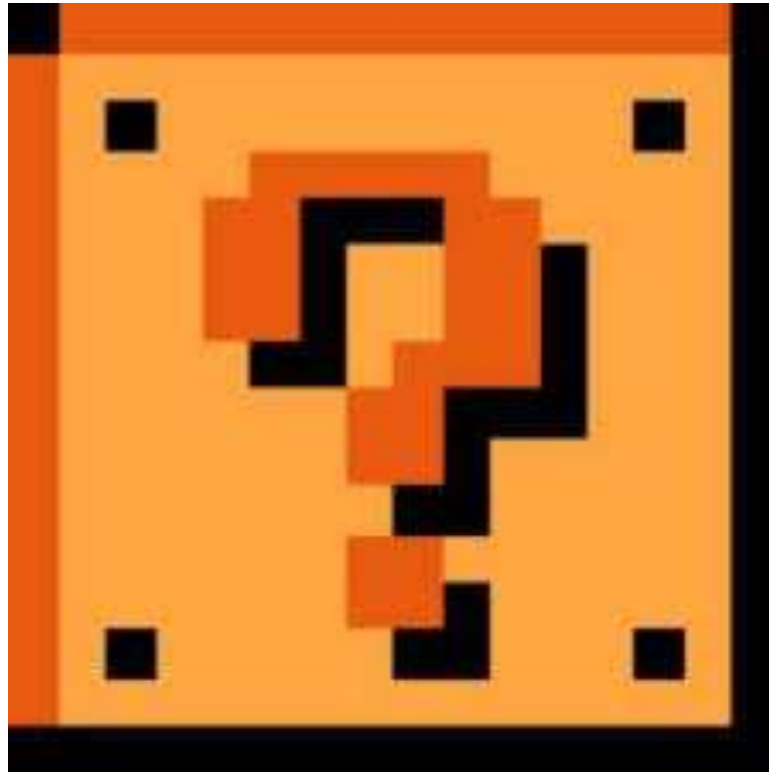








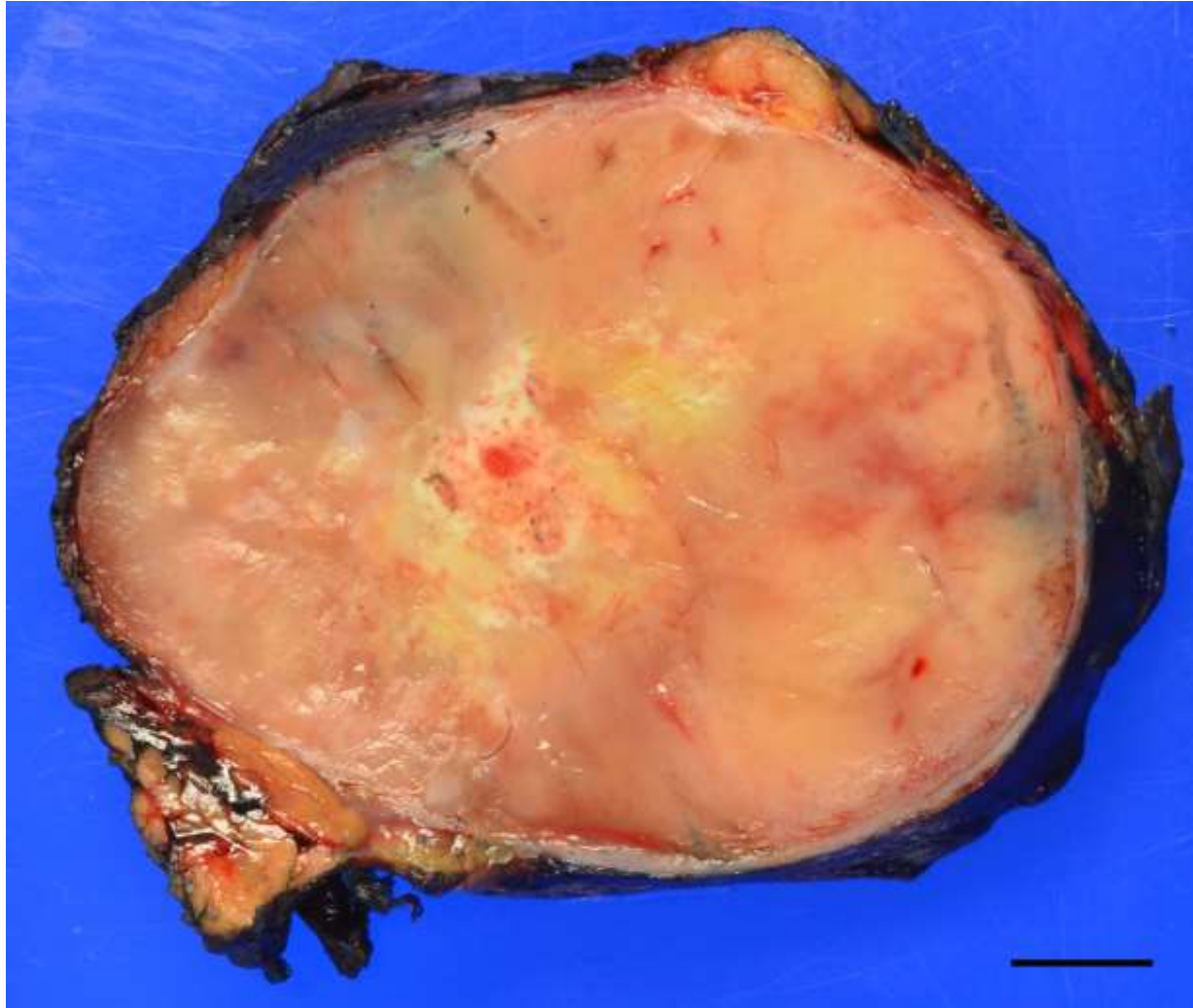
DIAGNOSIS?

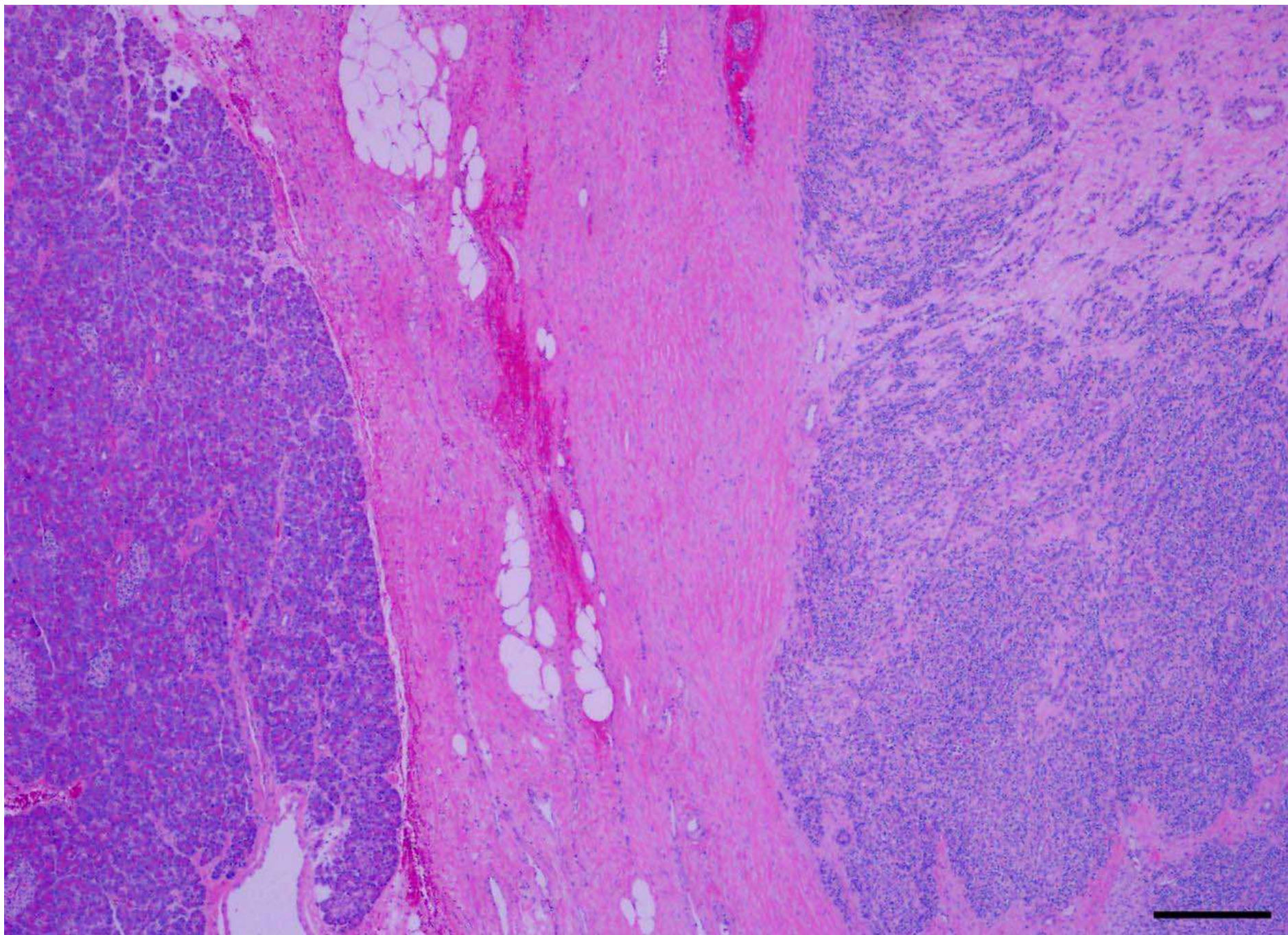


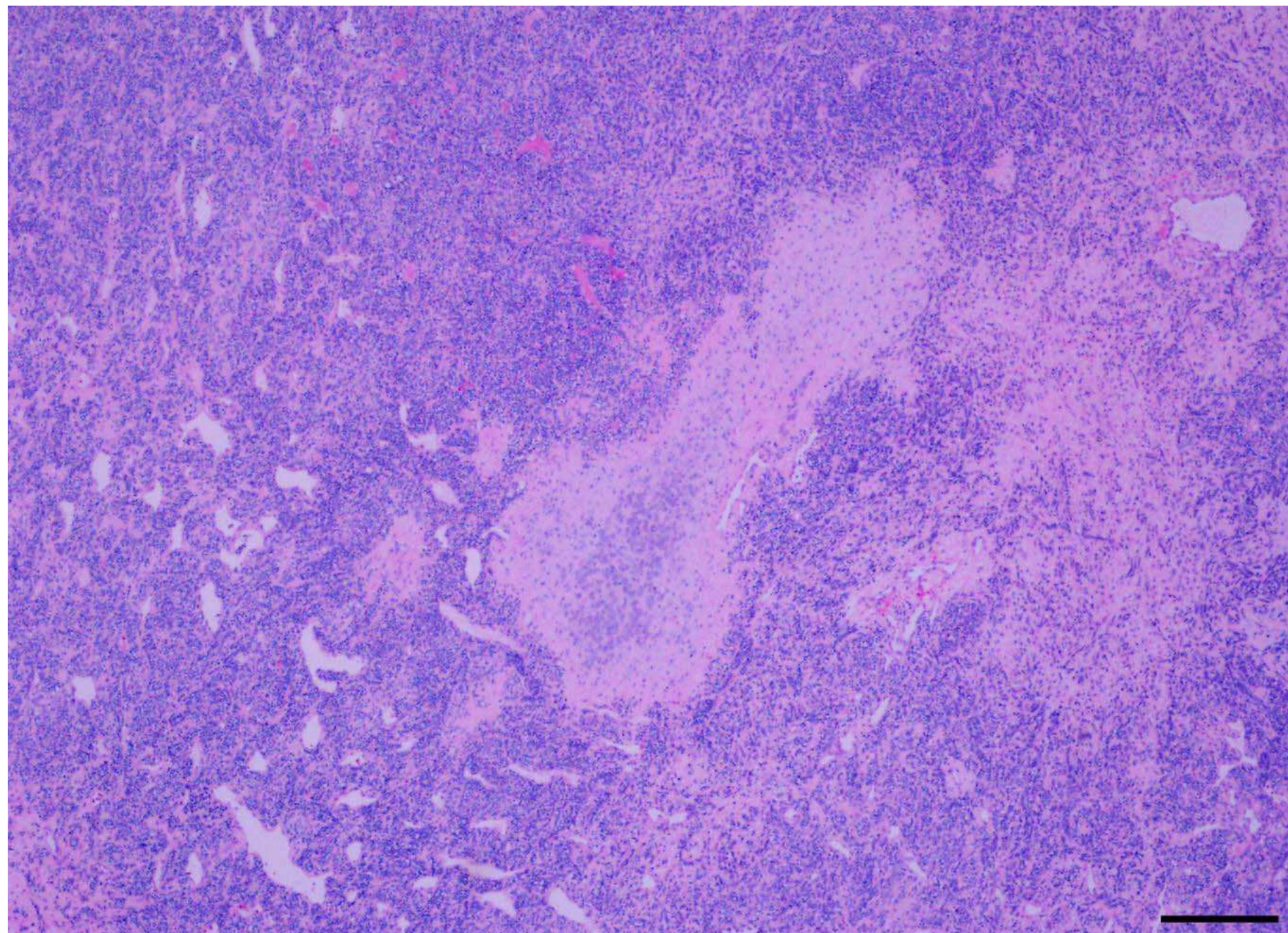
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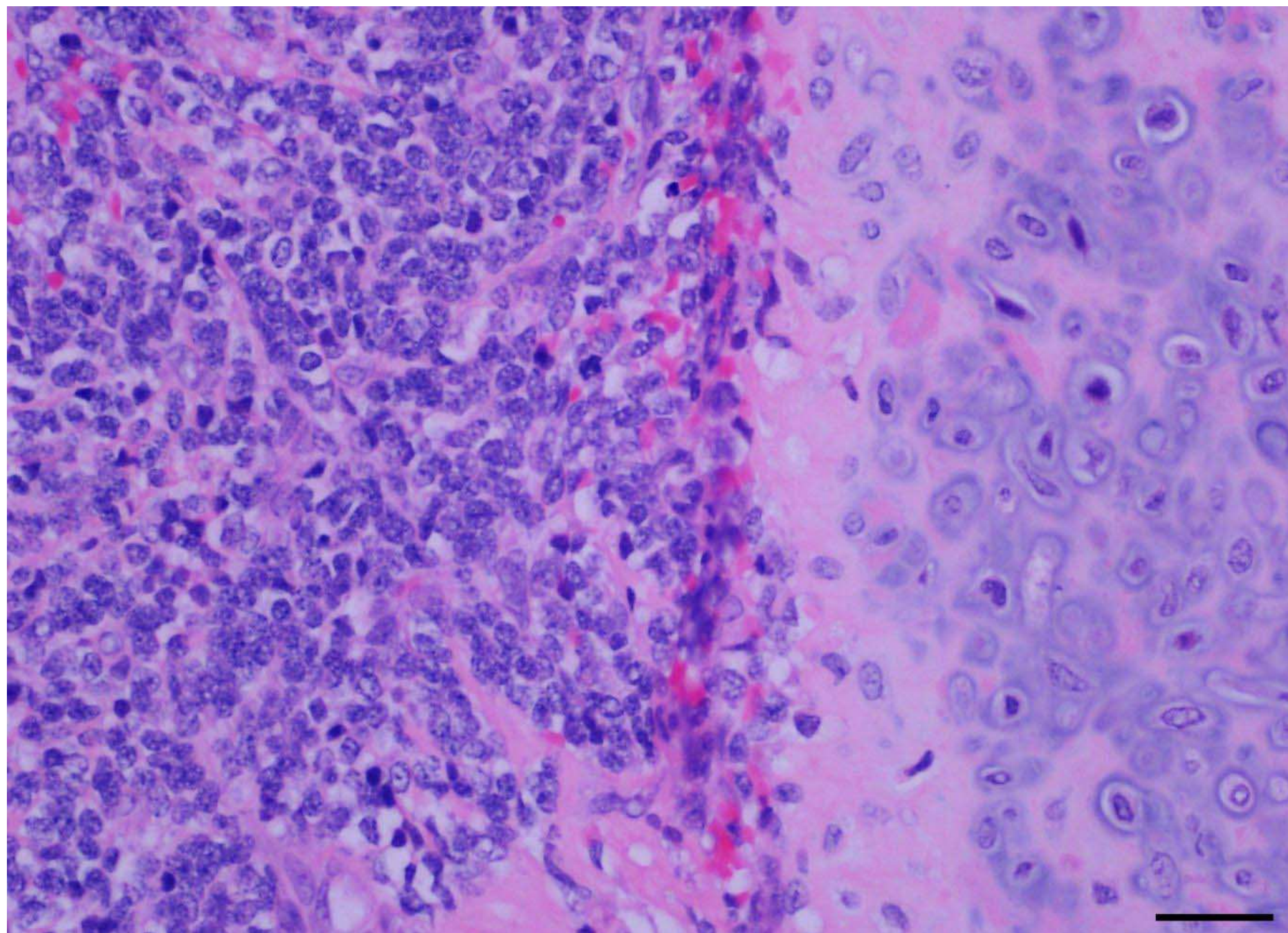


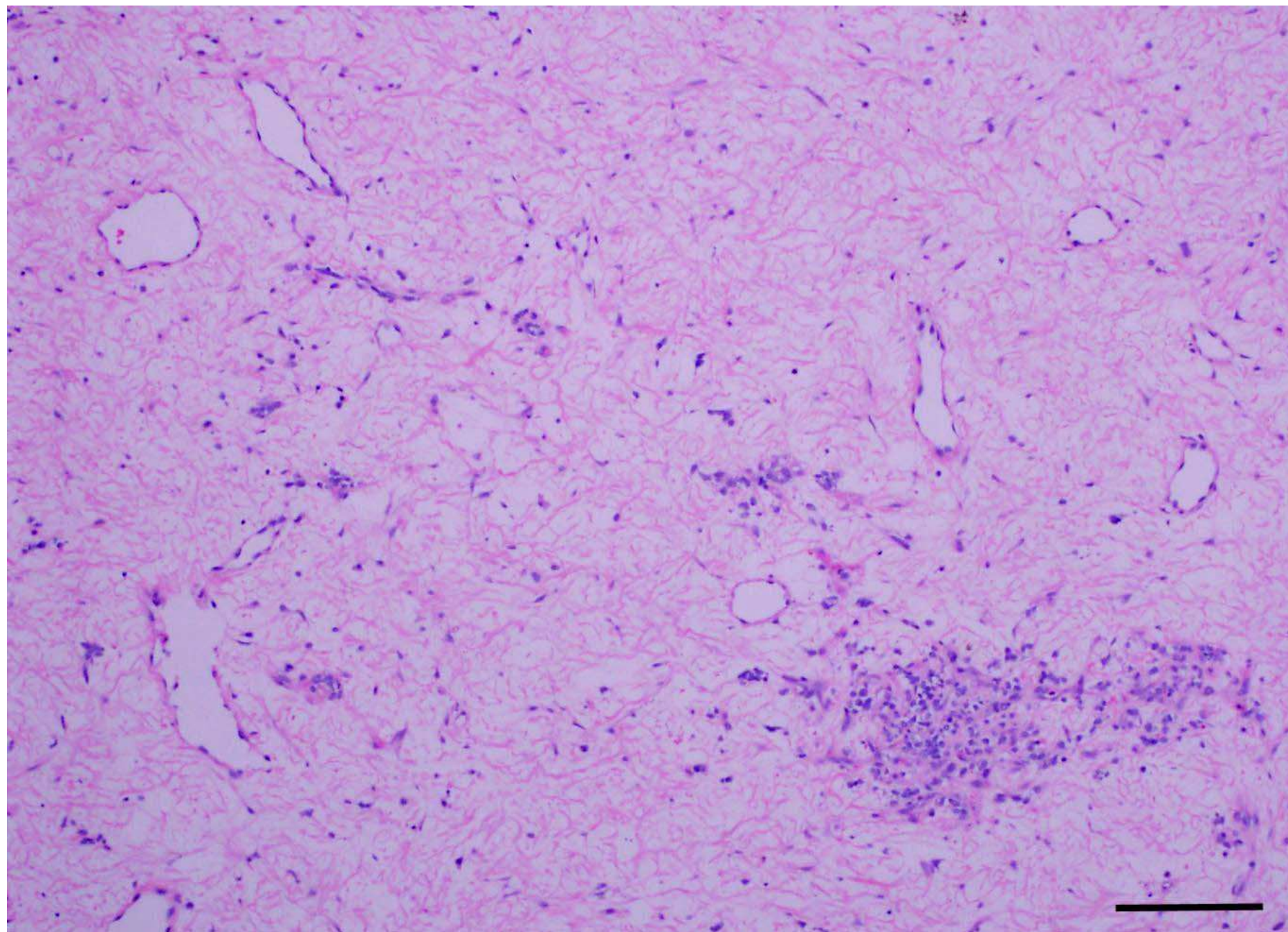
Gross Pathology

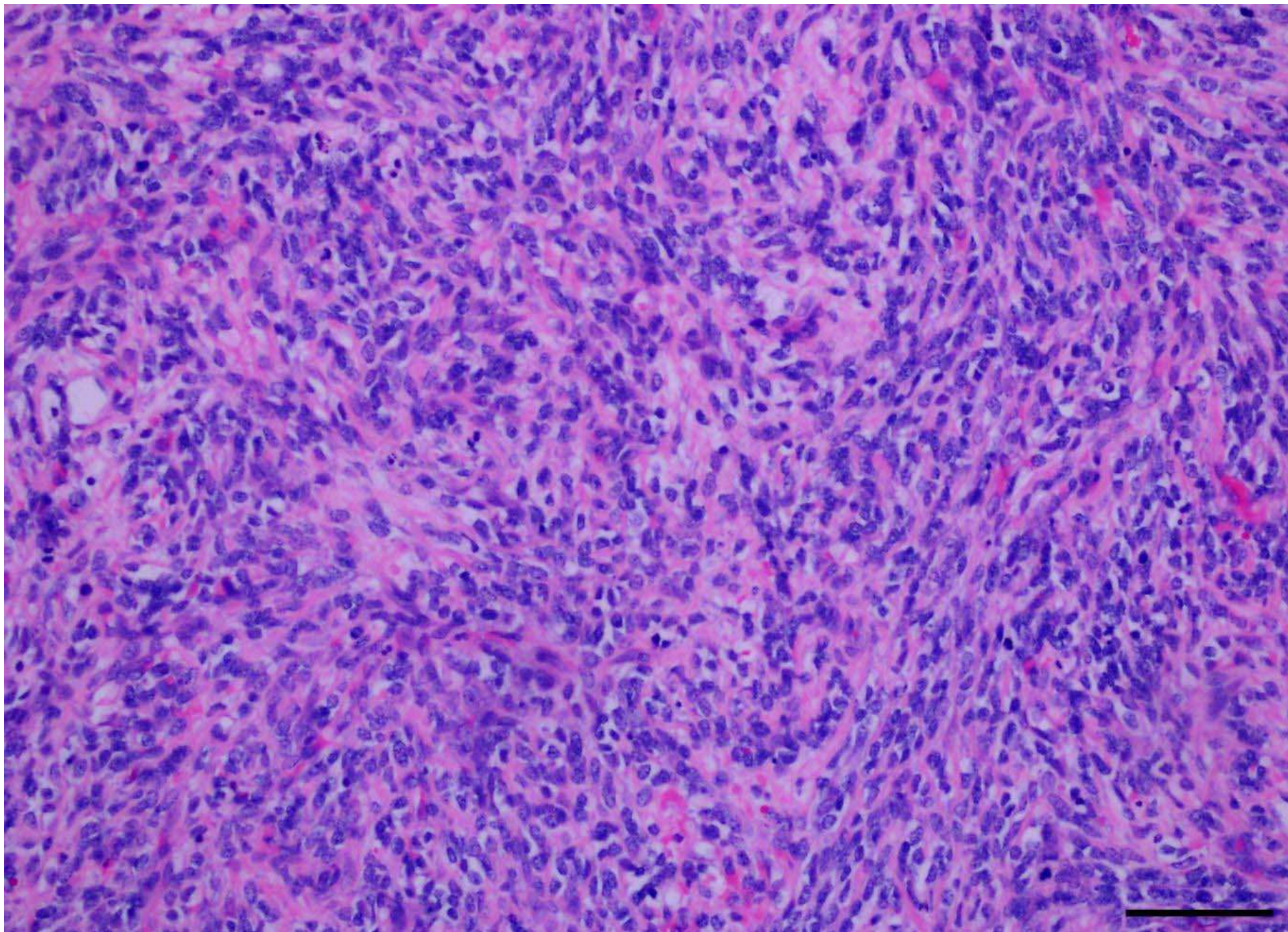




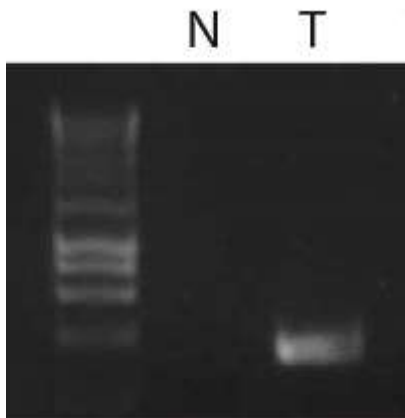






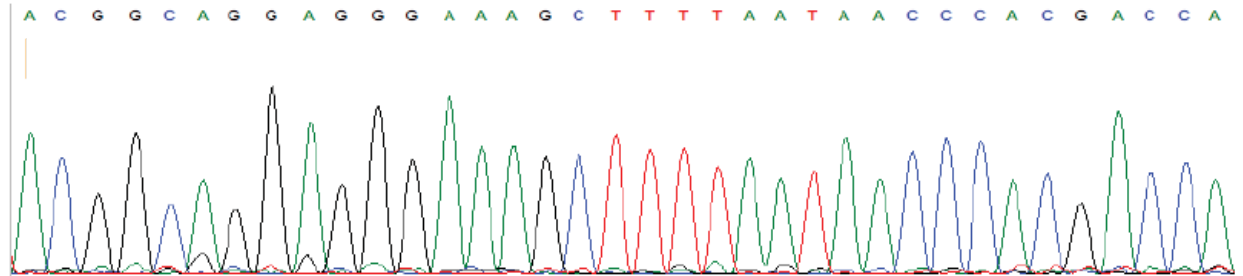


Molecular Studies



HEY1 exon 4

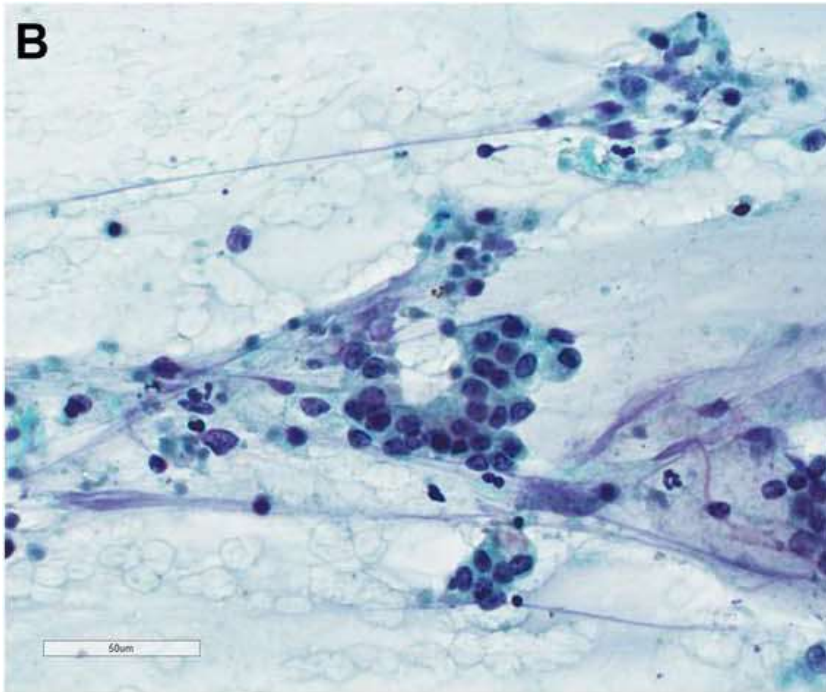
NCOA2 exon 13



Discussion

- Pancreas is a potential site of involvement by mesenchymal chondrosarcoma (2/8 cases in UCSF archives 1990-Present)
- HEY1-NCOA2 gene fusion is a recurrent genetic abnormality in MC (72% of cases)
- Molecular testing can be used as a diagnostic aid (potential for cytology material)

FNA of mesenchymal chondrosarcoma metastatic to pancreas



References

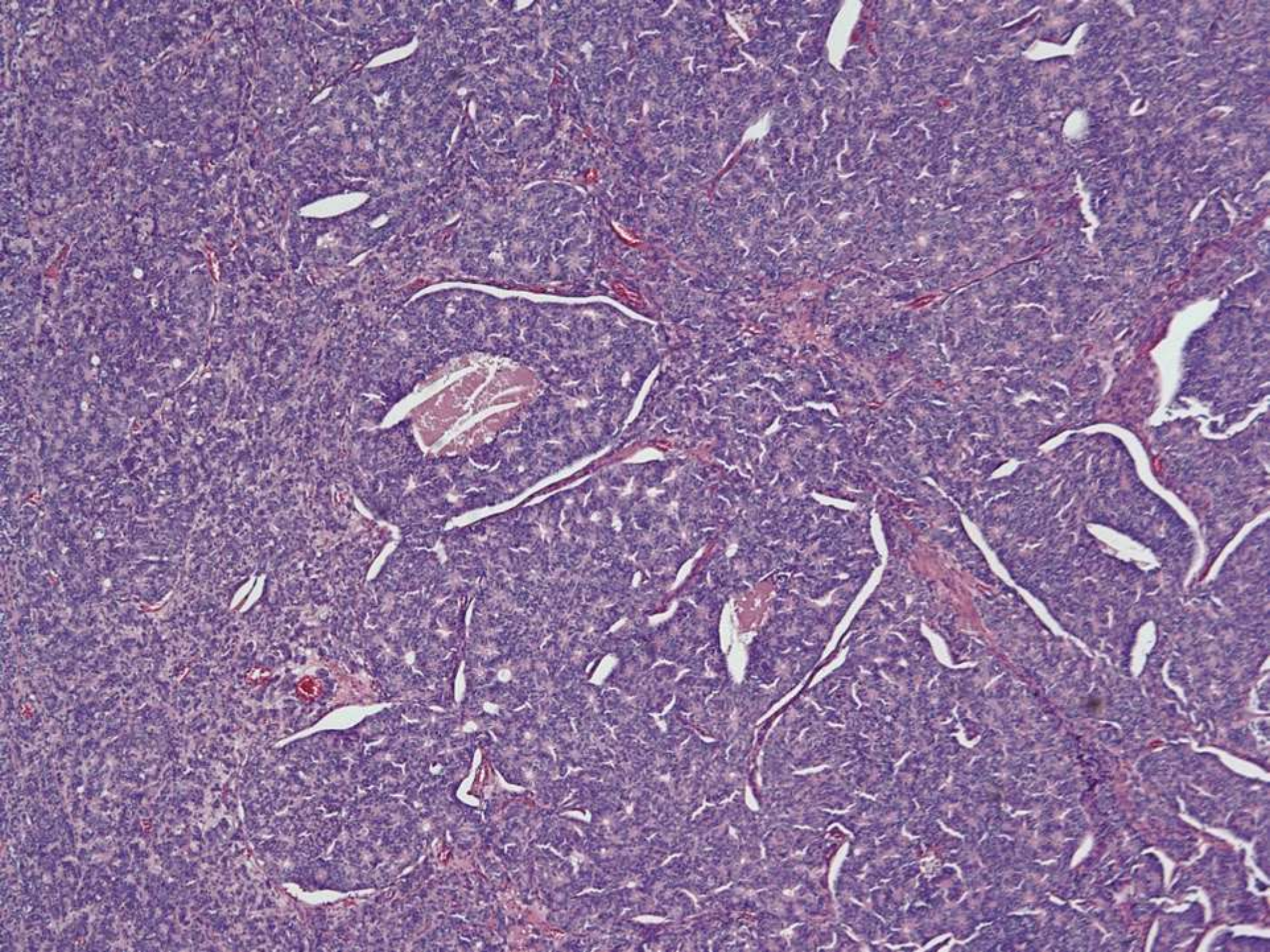
- Wang L, Motoi T, Khanin R, et al. *Identification of a novel, recurrent HEY1-NCOA2 fusion in mesenchymal chondrosarcoma based on a genome-wide screen of exon-level expression data.* Genes Chromosomes Cancer. 2012; 51(2):127-139.
- Chatzipantelis P, Karvouni E, Fragoulidis GP, et al. *Clinicopathologic features of two rare cases of mesenchymal metastatic tumors in the pancreas.* Pancreas. 2006; 33:301-303.
- Smith AL, Odronic SI, Spring BS, et al. *Solid tumor metastases to the pancreas diagnosed by FNA: A single-institution experience and review of the literature.* Cancer Cytopathol. 2015; 123:347-355.

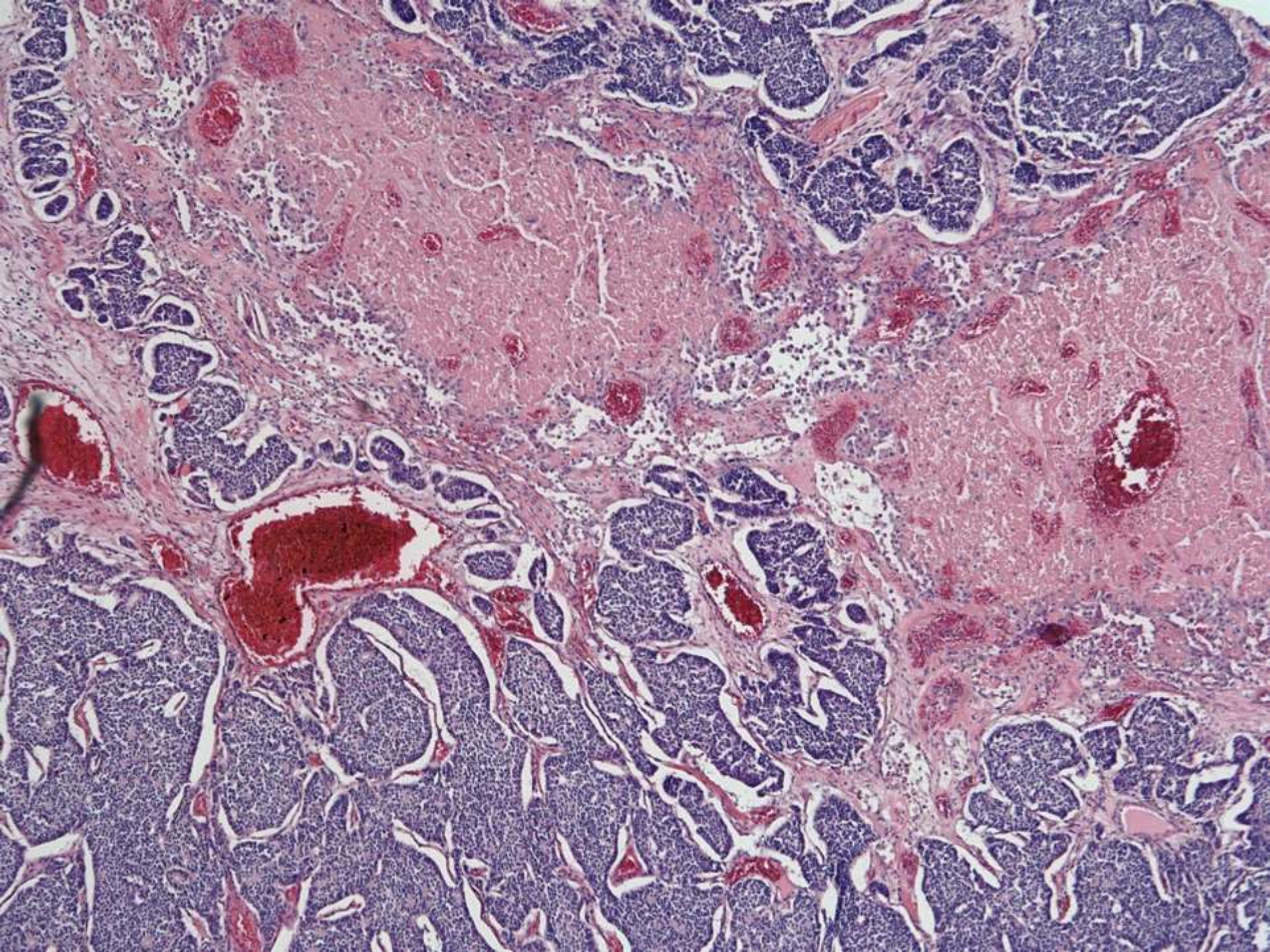
SB 6042

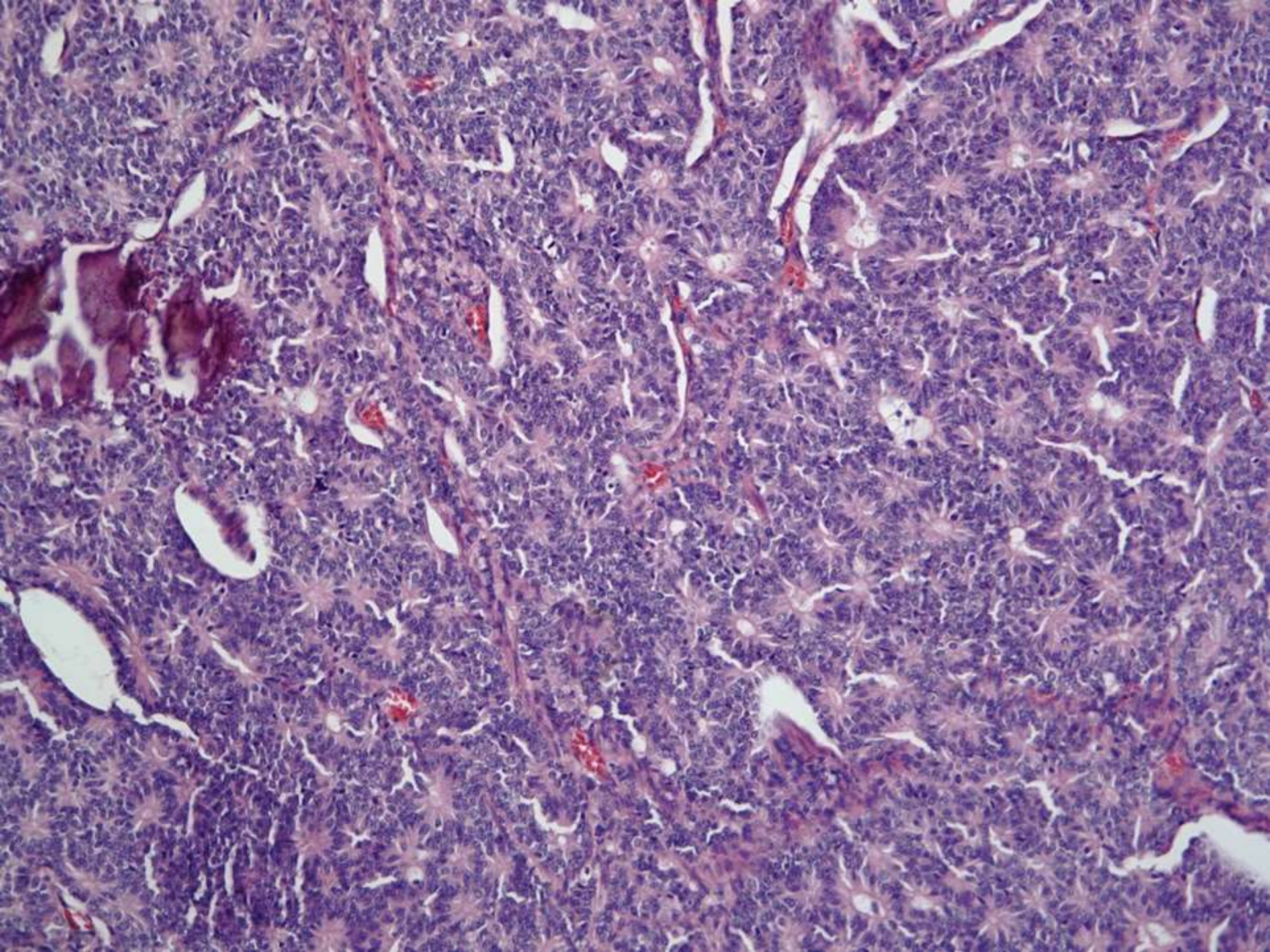
Greg Charville/Robert Rouse; Stanford & Palo Alto VA

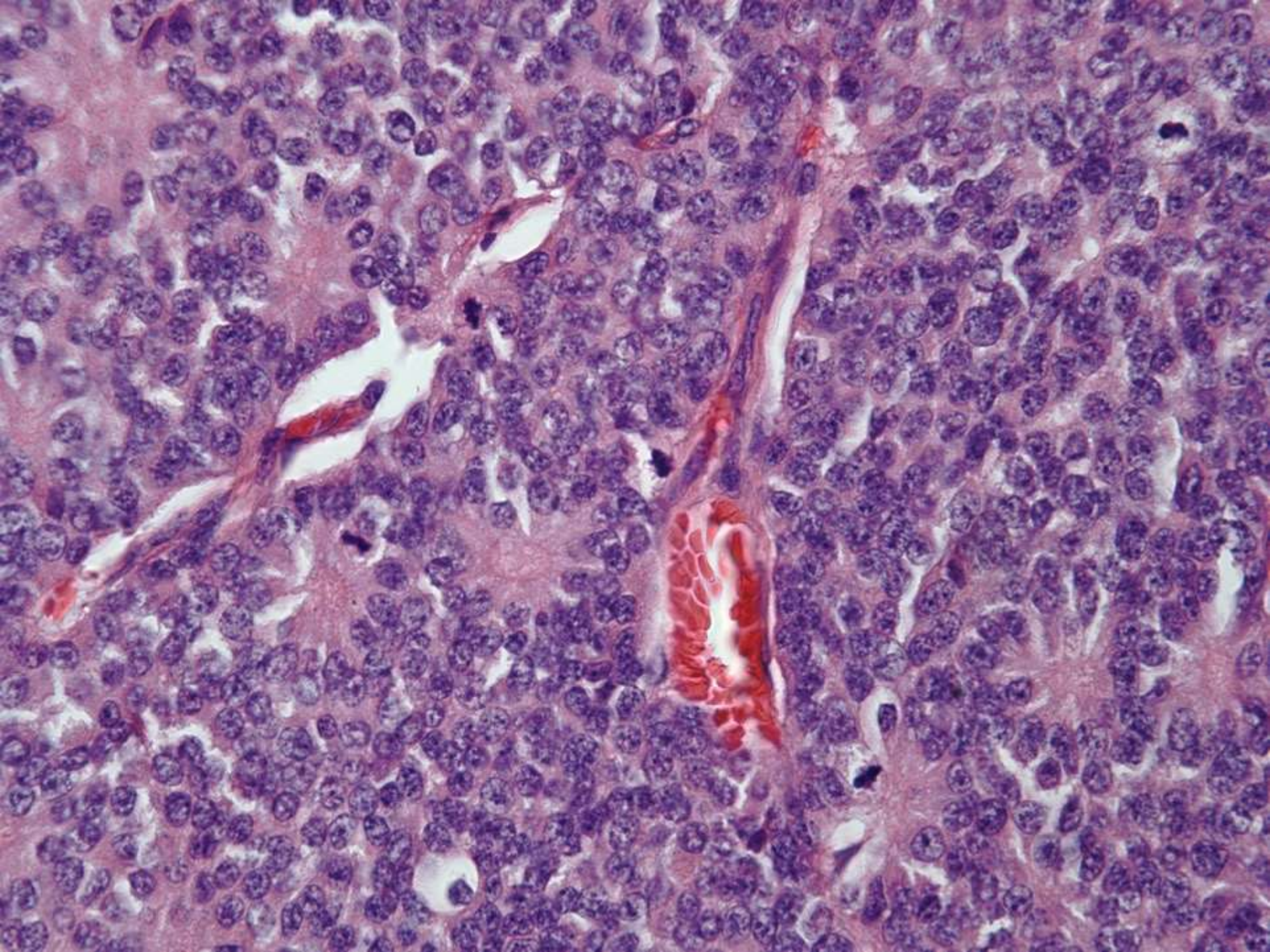
39-year-old man with an anterior mediastinal mass.

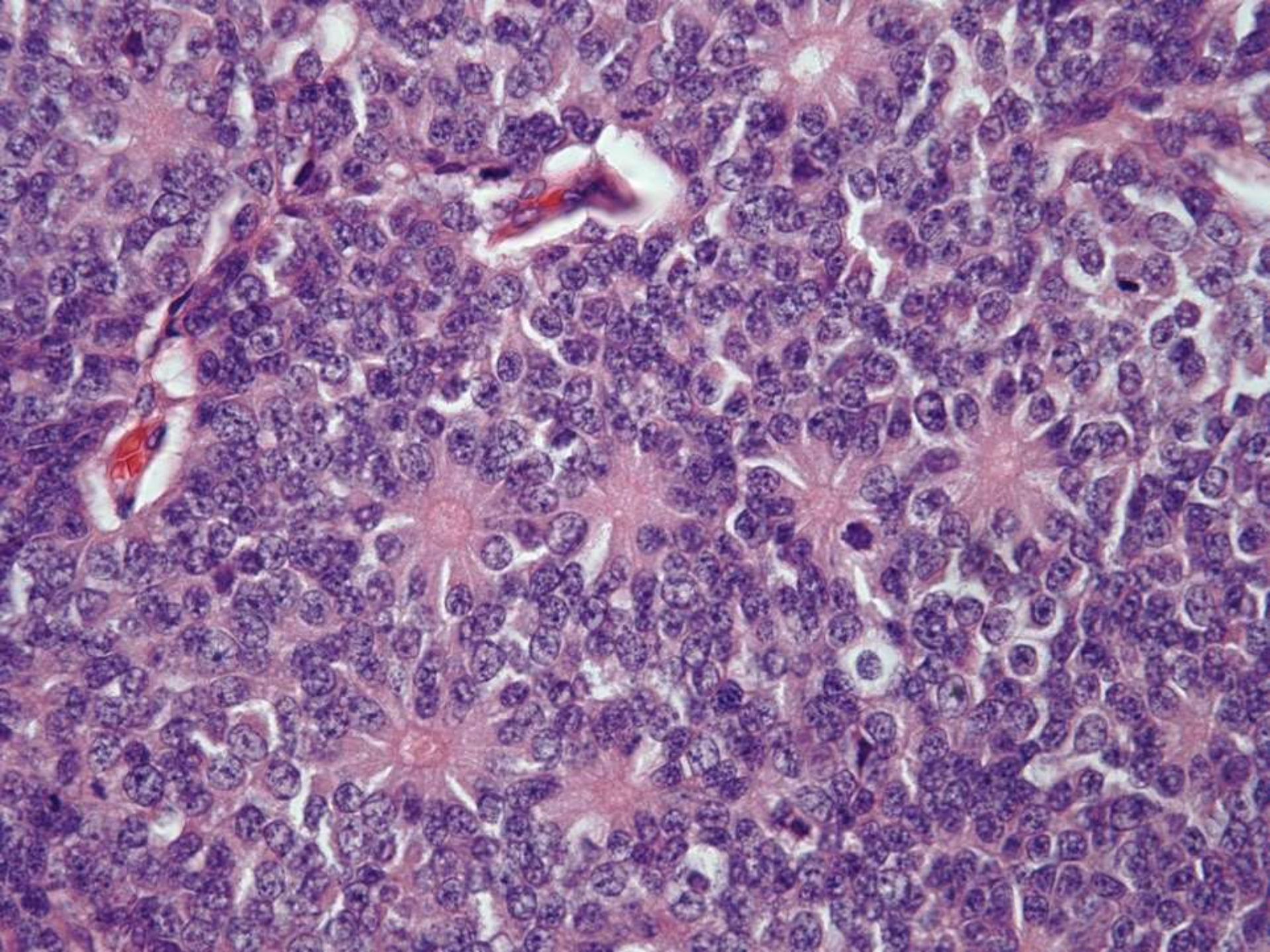
How would you grade this cancer?







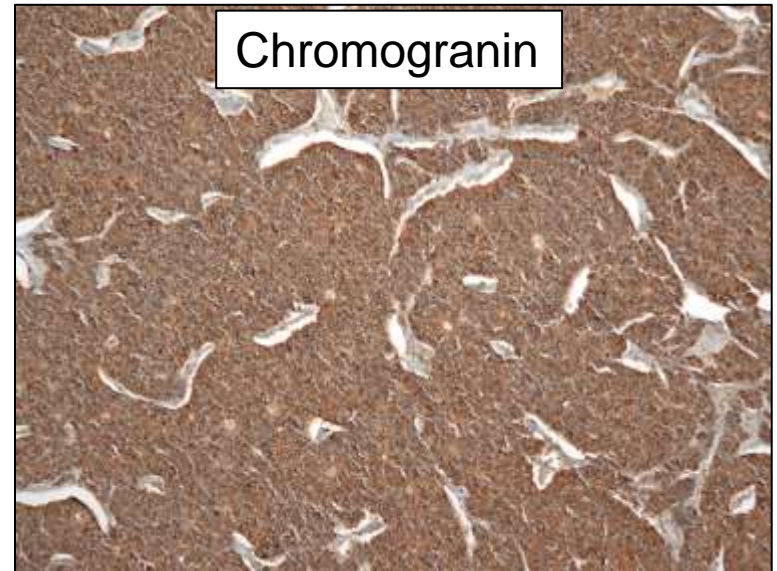
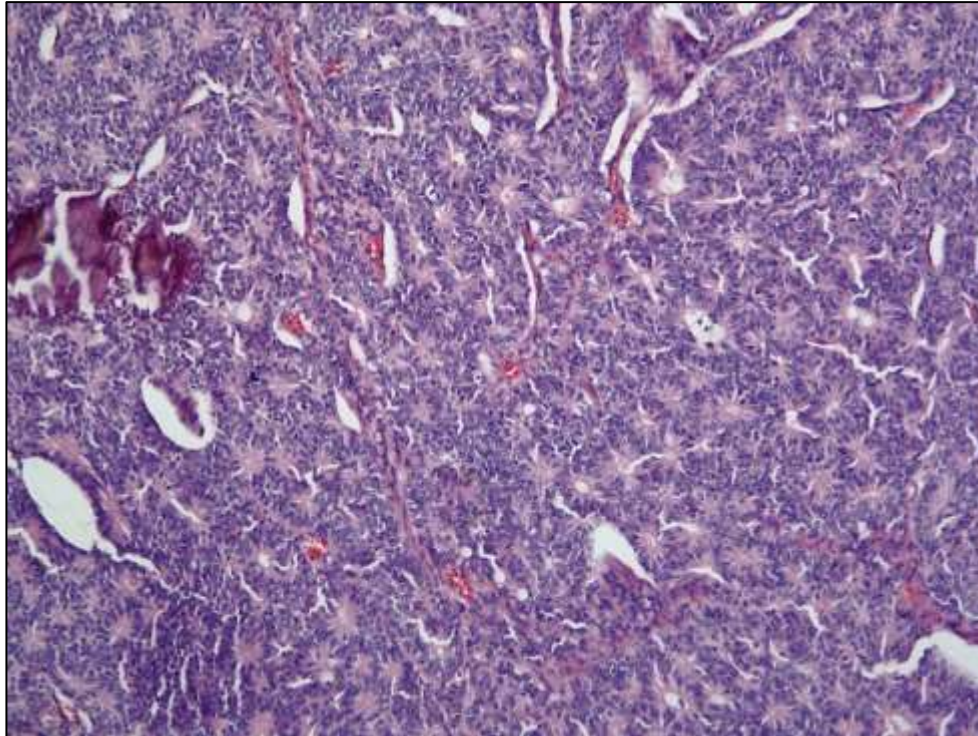




DIAGNOSIS?



Thymic neuroendocrine tumor



Thymic neuroendocrine tumor

- Thymic epithelial tumor showing expression of more than one neuroendocrine marker in greater than 50% of cells (with the exception of small cell carcinoma)
- Annual incidence: 0.2 per million (representing 2-5% of thymic tumors and 0.4% of carcinoid tumors)
- Most present with symptoms of local progression (cough, dyspnea, SVC syndrome) or Cushing syndrome (due to ectopic ACTH)
- 25% of thymic NETs associated with MEN-1

What's in a name? – Grading thymic NETs

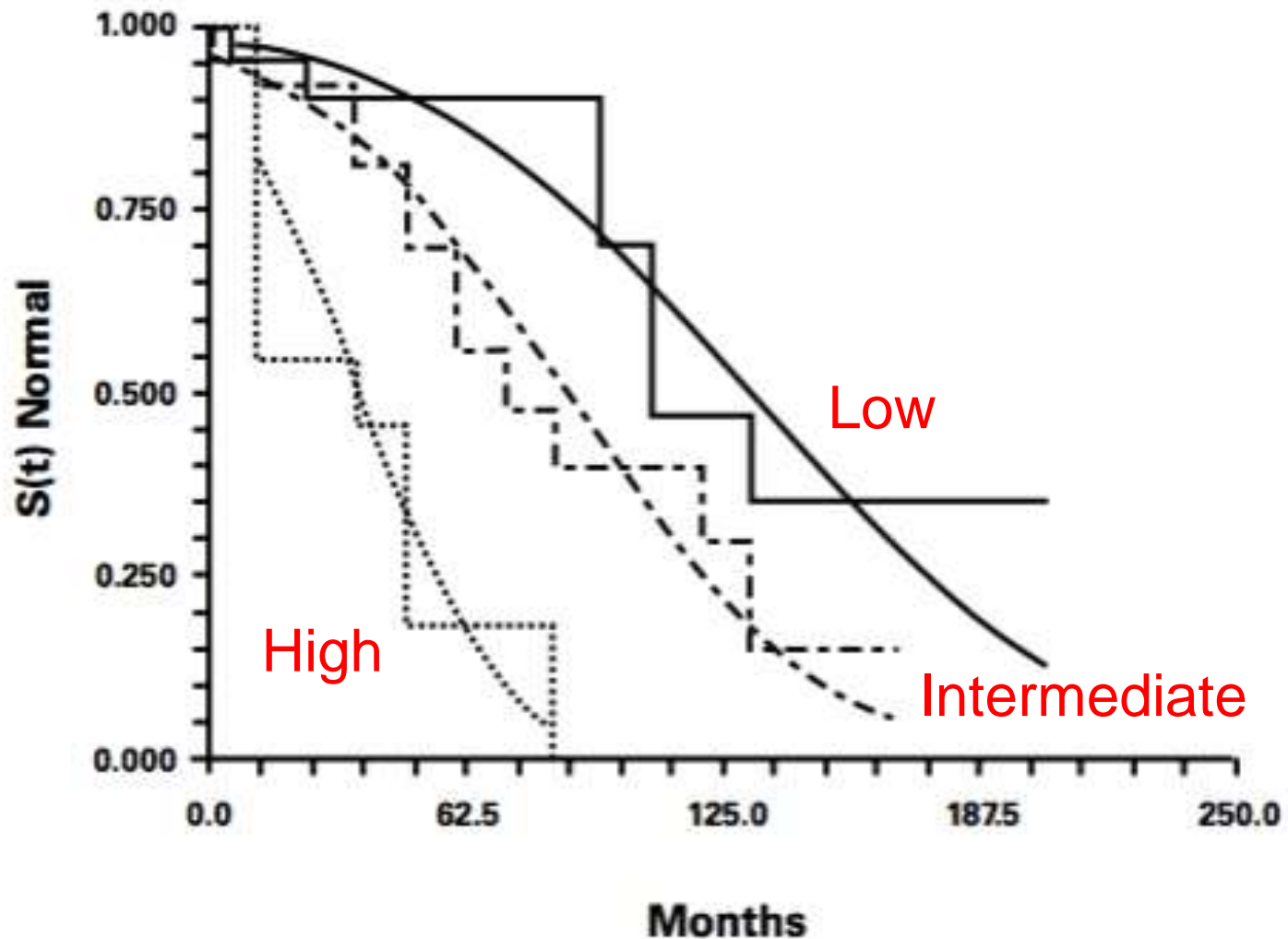
Classification of thymic neuroendocrine tumours (Neuroendocrine carcinomas, NECs) {1691}.

Neuroendocrine Carcinomas (NECs)			
Well-differentiated NEC Neuroendocrine Tumors		Poorly differentiated NEC High-grade (carcinomas)	
<i>Typical Carcinoid</i> Low-grade No necrosis; <2 mitoses per 2 mm ² (10HPF)	<i>Atypical Carcinoid</i> Intermediate-grade Necrosis present and/or 2-10 mitoses per 2 mm ² (10 HPF)	<i>LCNEC*</i> Non-small cell NEC with >10 mitoses per 2 mm ² (10 HPF)	<i>SCC**</i> Small cell cytology
<i>Morphological Variants</i> Spindle cell type Pigmented type With amyloid (extrathyroidal medullary carcinoma) Oncocytic/oxyphilic type Mucinous Angiomatoid type Combinations of the above variants			<i>Variants</i> SCNEC combined with Non-NECs
Thymic NECs with shared features of (atypical) carcinoid and LCNEC/SCC Carcinoid with sarcomatous change ("metaplastic NEC")			

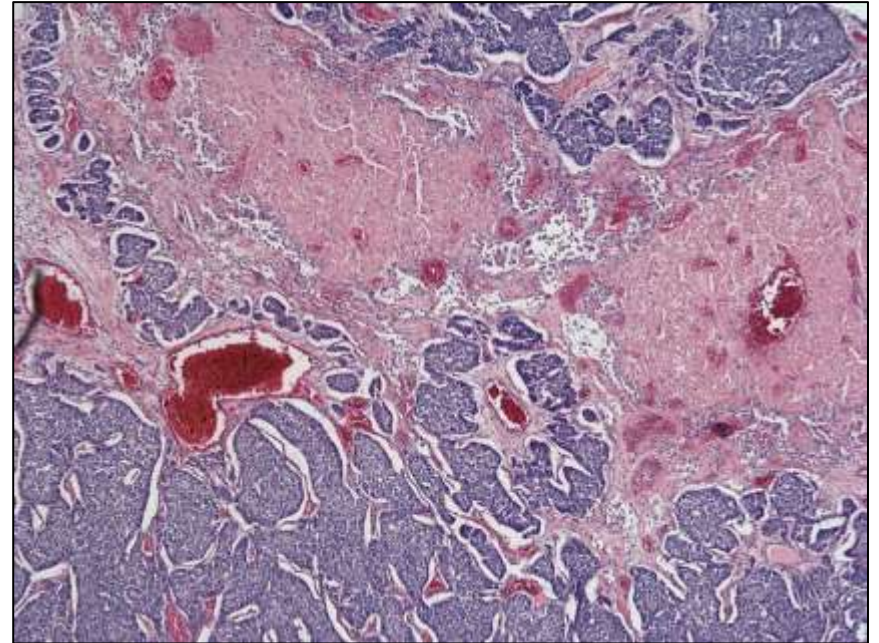
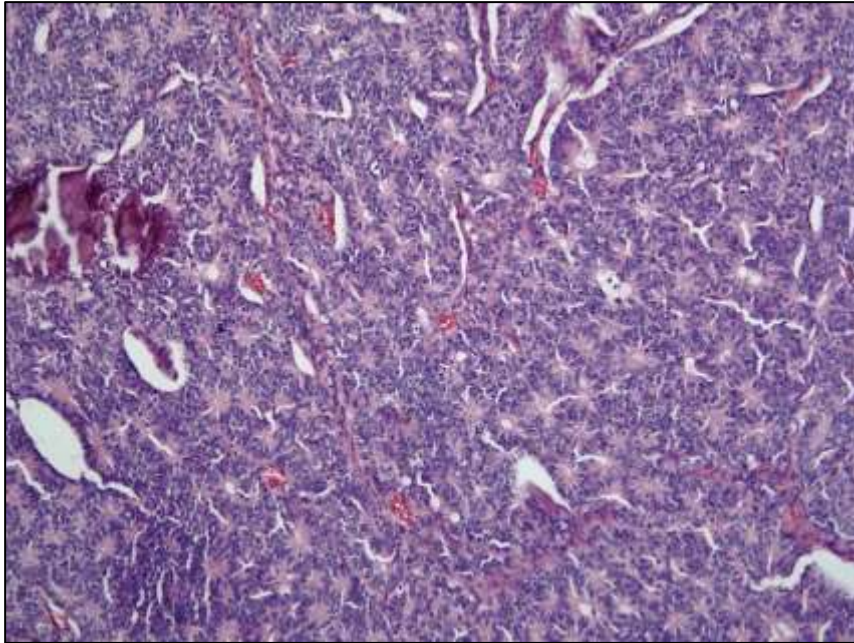
*LCNEC, large cell neuroendocrine carcinoma;

**SCC, small cell carcinoma; HPF, high power field

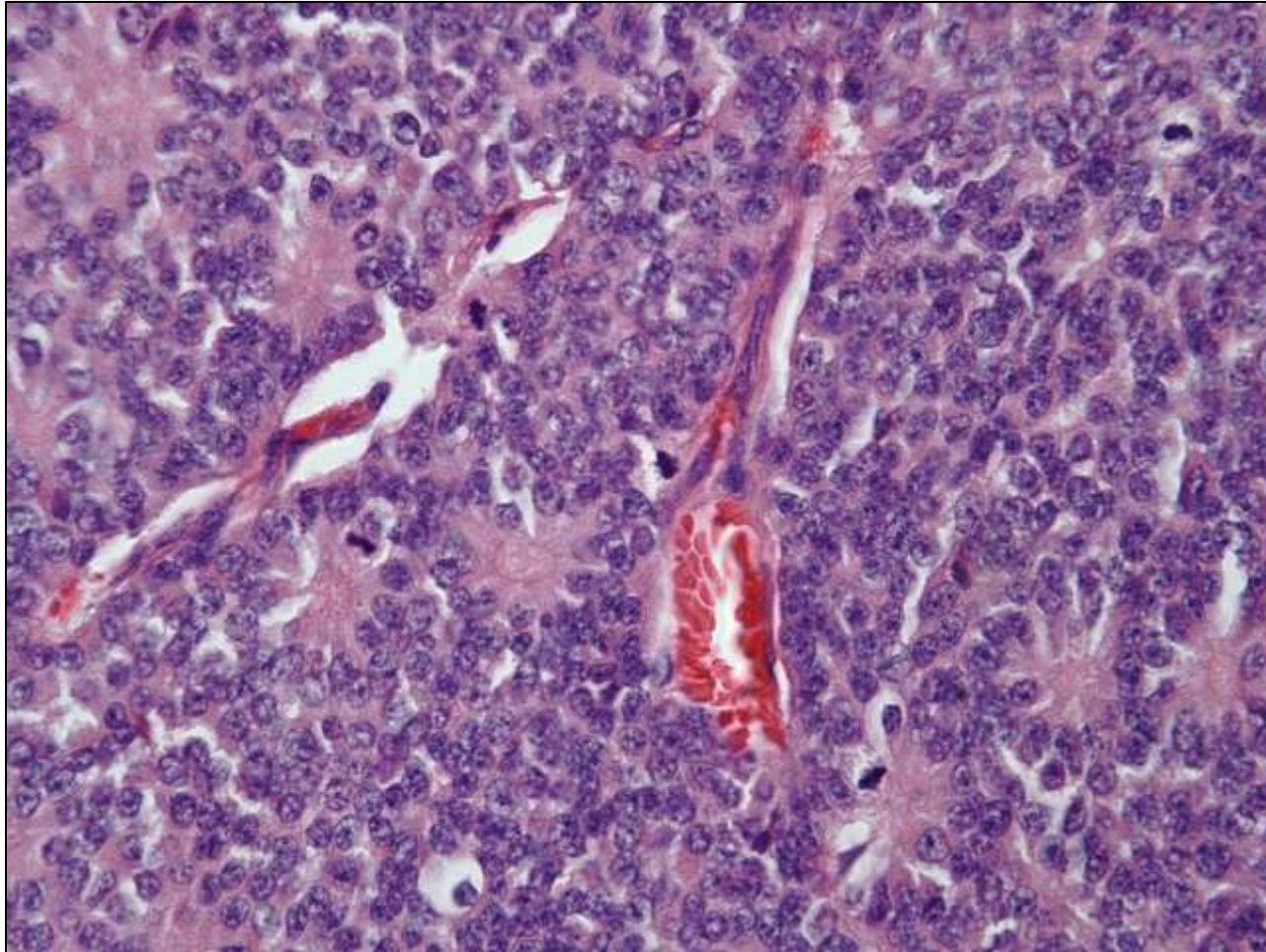
Thymic neuroendocrine tumors – clinical outcomes



Thymic neuroendocrine tumors – our case



Thymic neuroendocrine tumors – our case



“A higher mitotic rate is the essential differentiating feature of LCNEC from atypical carcinoid.”

Our case: clinical follow-up

2007: New-onset hypertension and diabetes, suspected pituitary microadenoma, underwent transsphenoidal resection (pathology showed normal pituitary)

July 2009 : Further work-up revealed mediastinal mass, underwent **primary tumor resection** with positive margins, metastasis to one LN (followed by XRT to tumor bed)

November 2014: Staging CT – T7/T9 paraspinal metastasis, metastasis to supraclavicular LN

July 2015: Excisional biopsy of supraclavicular LN, pathology shows involvement by NEC

November 2015: Plan for XRT to known lesions, octreotide tx, and repeat imaging

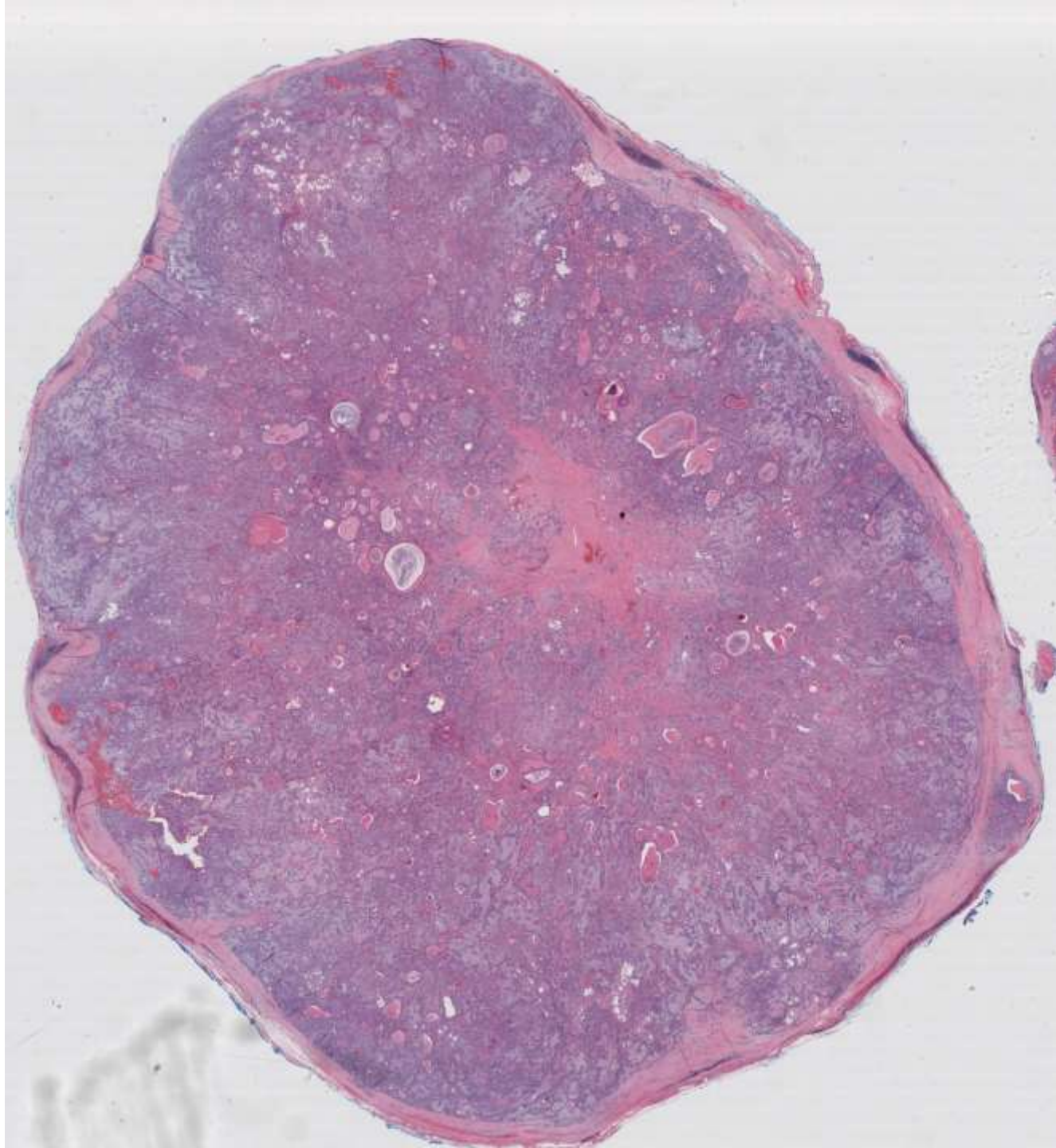
Thymic neuroendocrine tumors – take home points

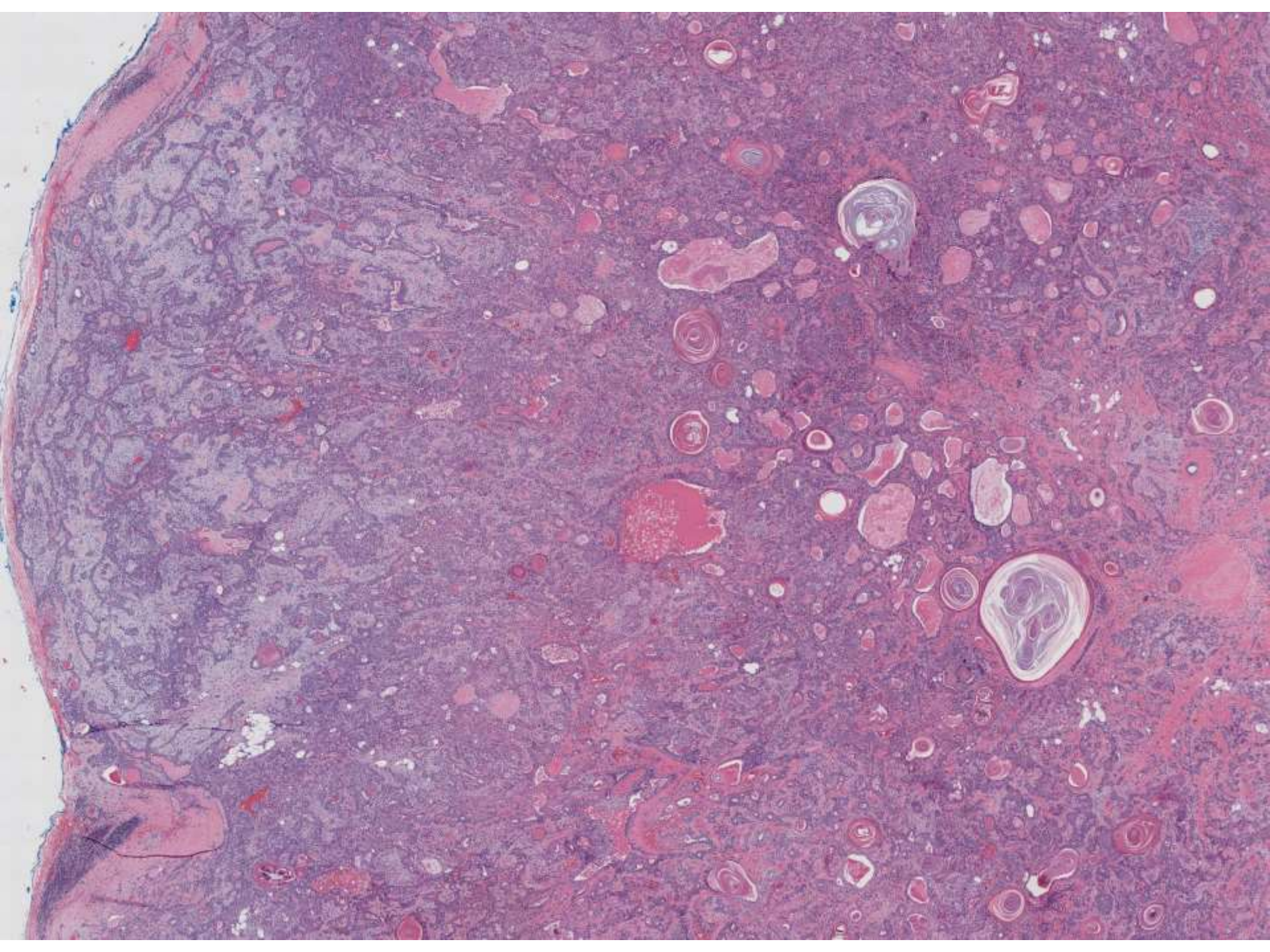
- 2015 WHO guidelines change nomenclature, but not criteria
- Changes reflect favored terminology of pulmonary NETs/NECs
- Histologic grading may help to predict clinical behavior of thymic NETs/NECs
- However, relative to counterparts arising elsewhere, thymic NETs/NECs typically are of a higher grade and show less favorable clinical behavior

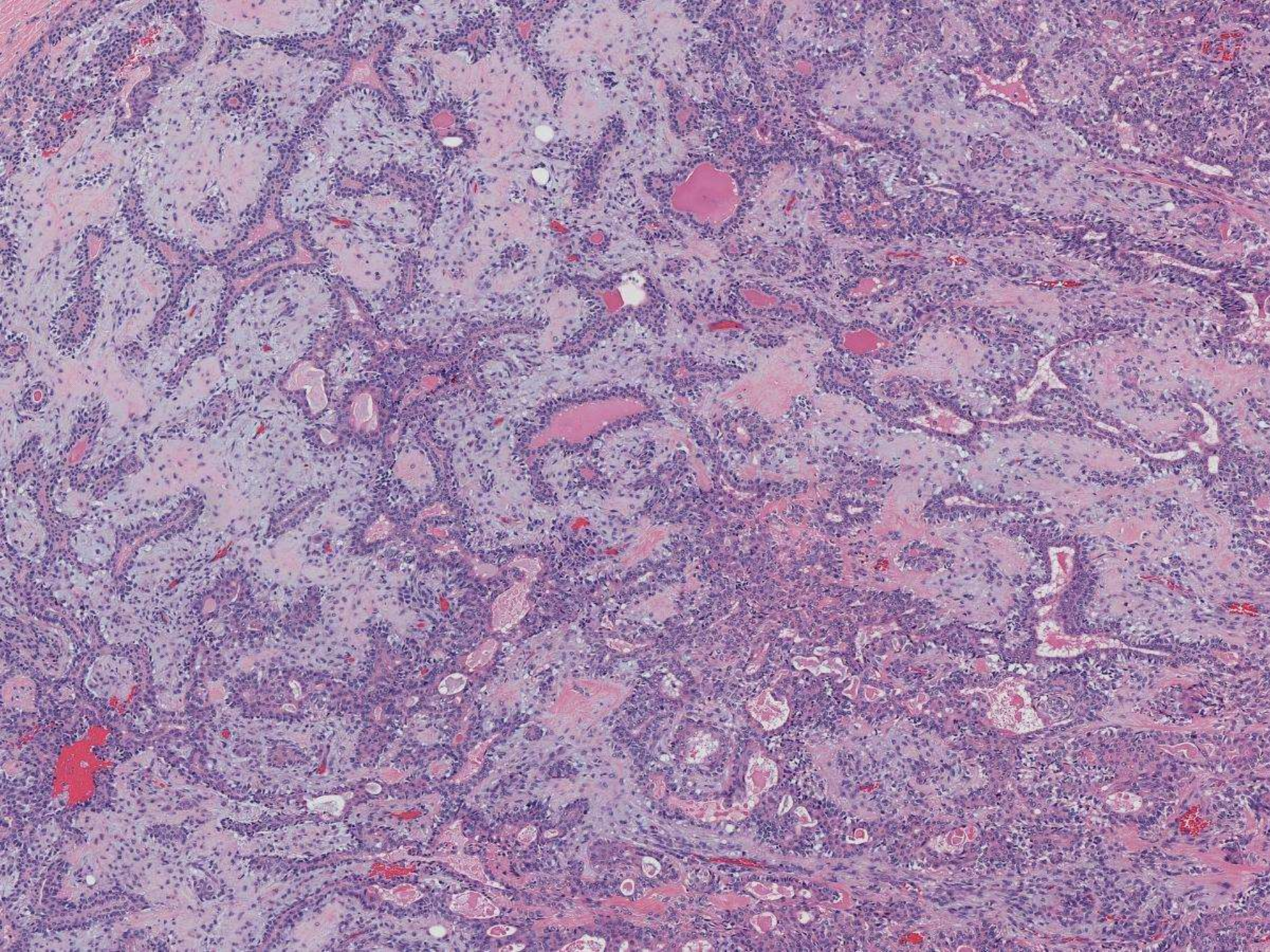
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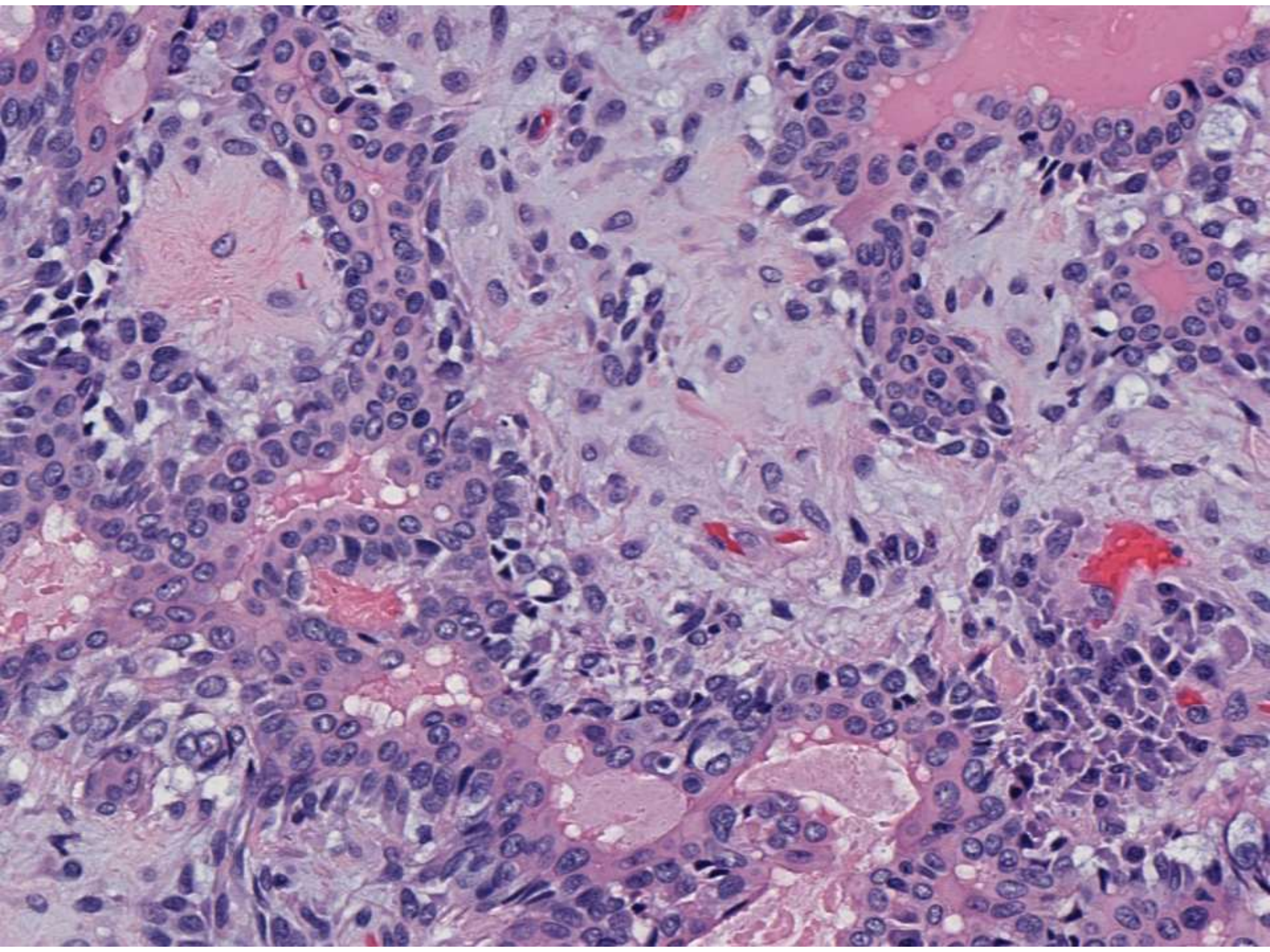
Balaram Puligandla; Kaiser Oakland

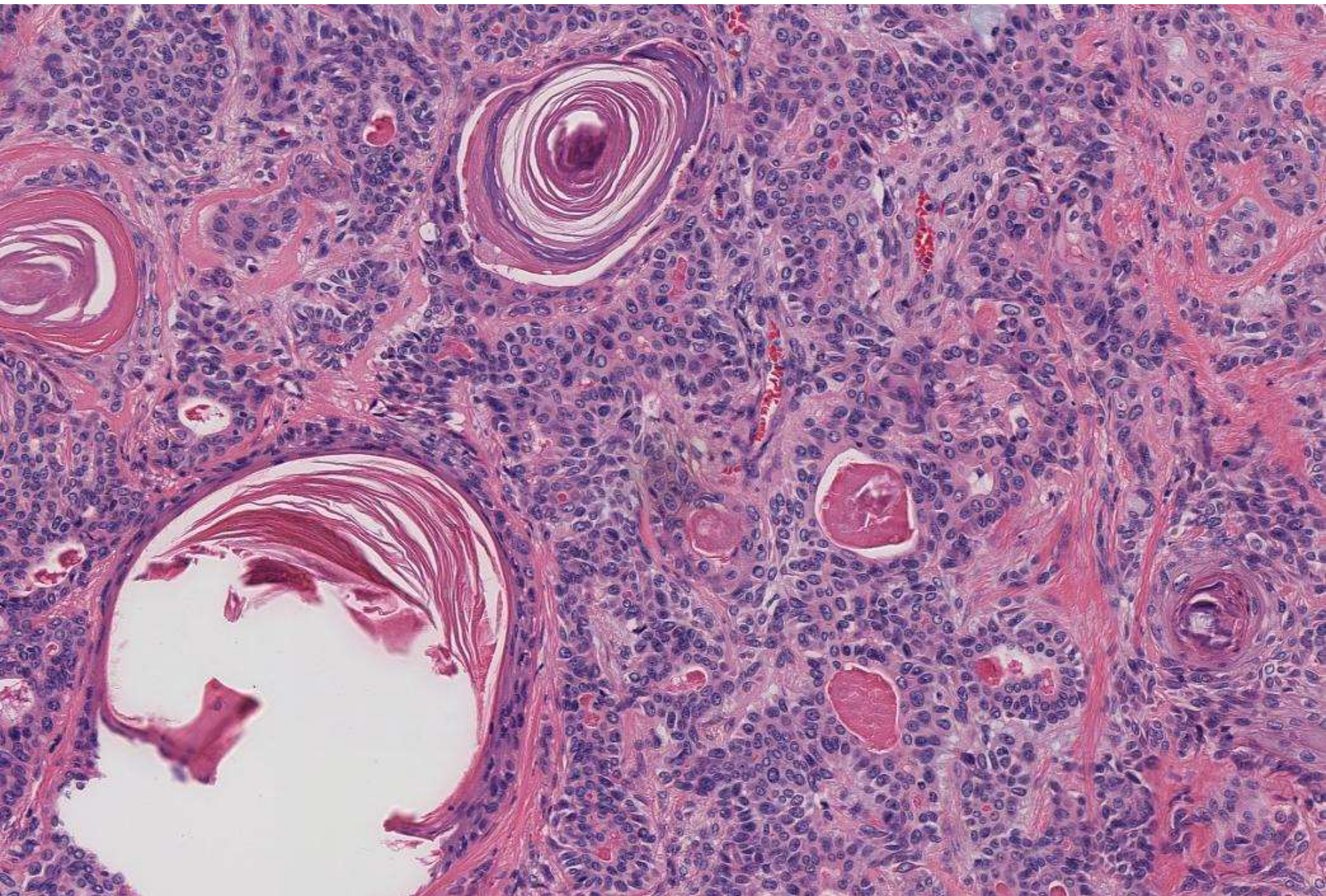
22-year-old male with long history of left lid ptosis and recent blurred vision was found to have left eye proptosis and globe displacement. CT shows 2cm mass in UOQ of left orbit with inferior displacement and proptosis of globe of eye.

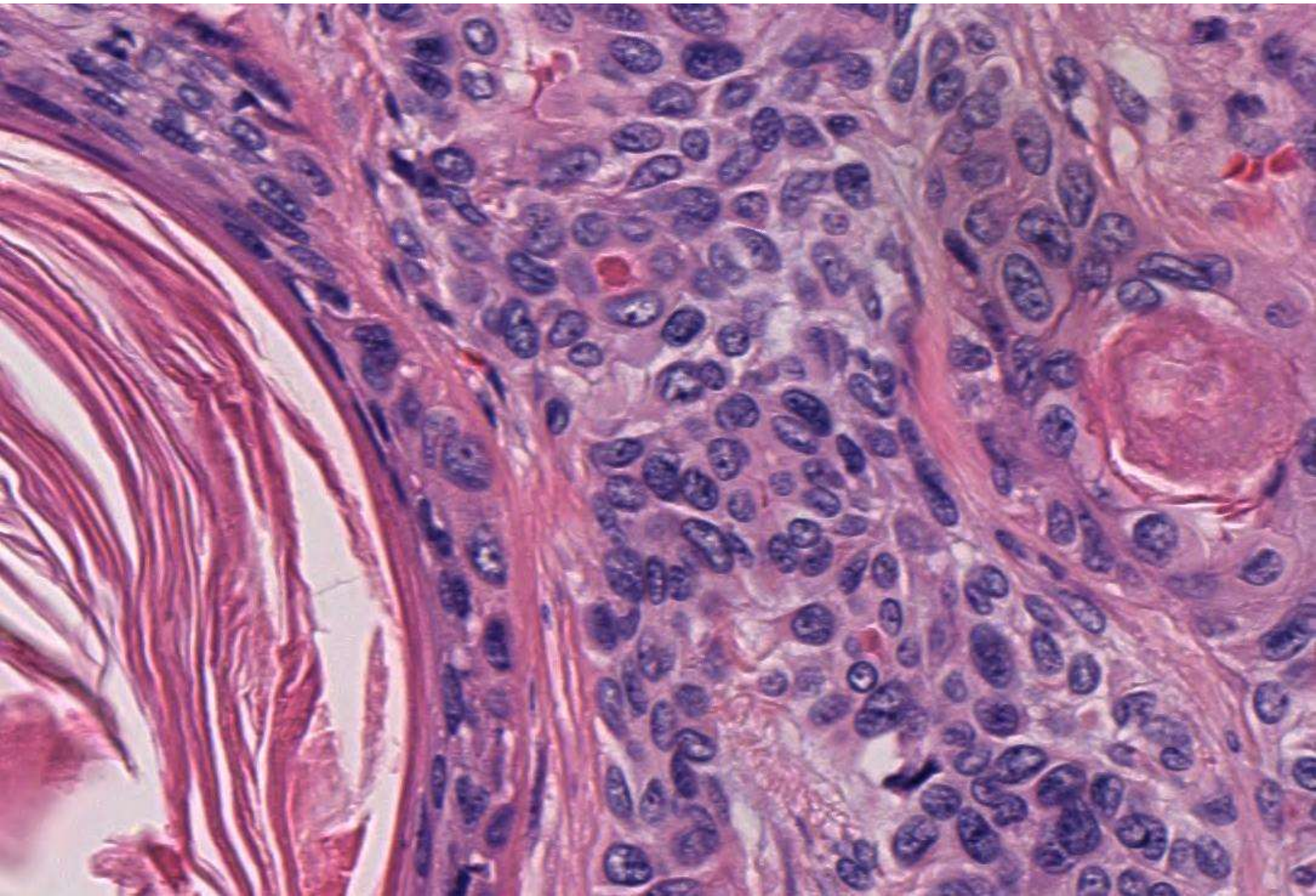


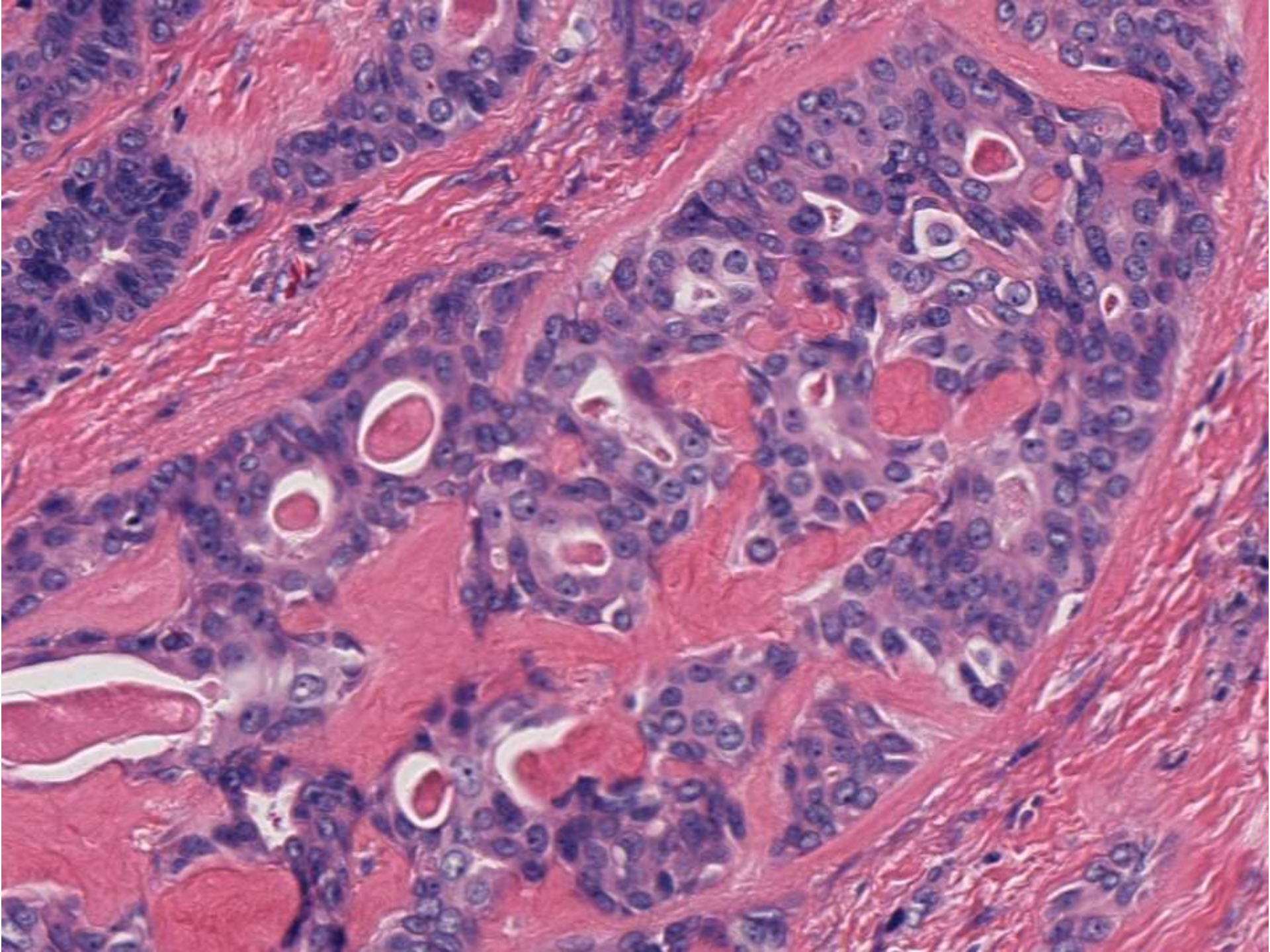


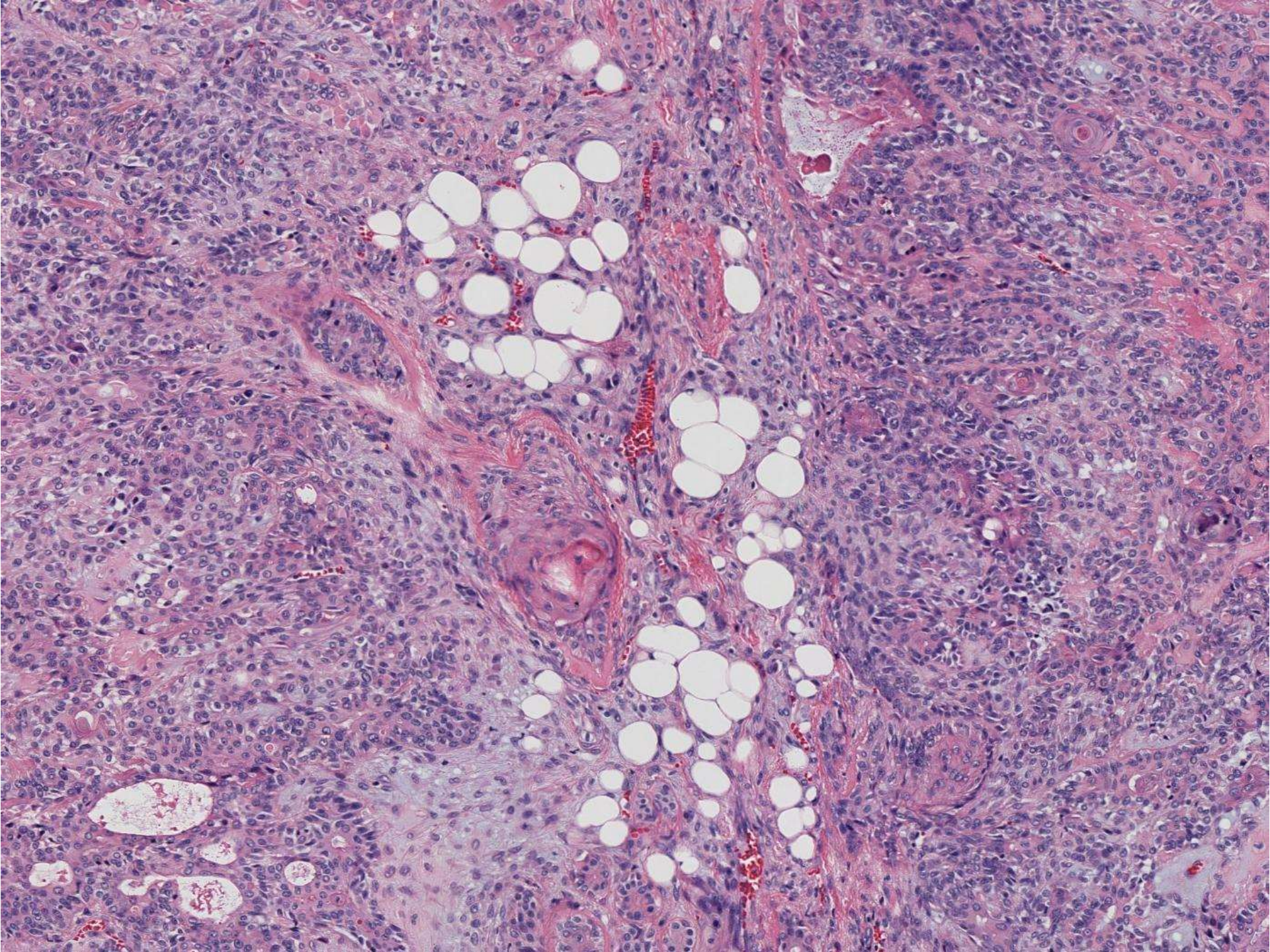


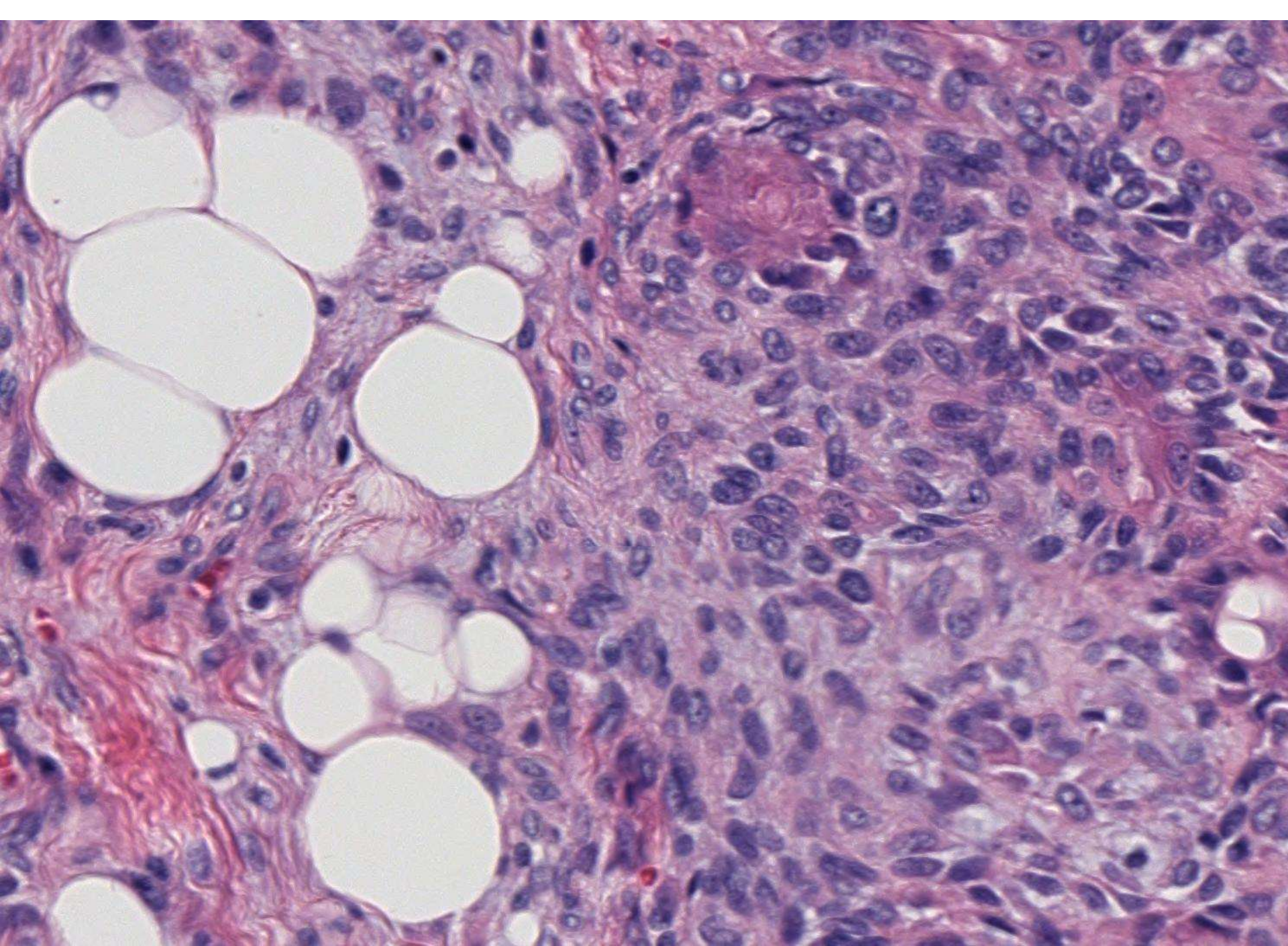




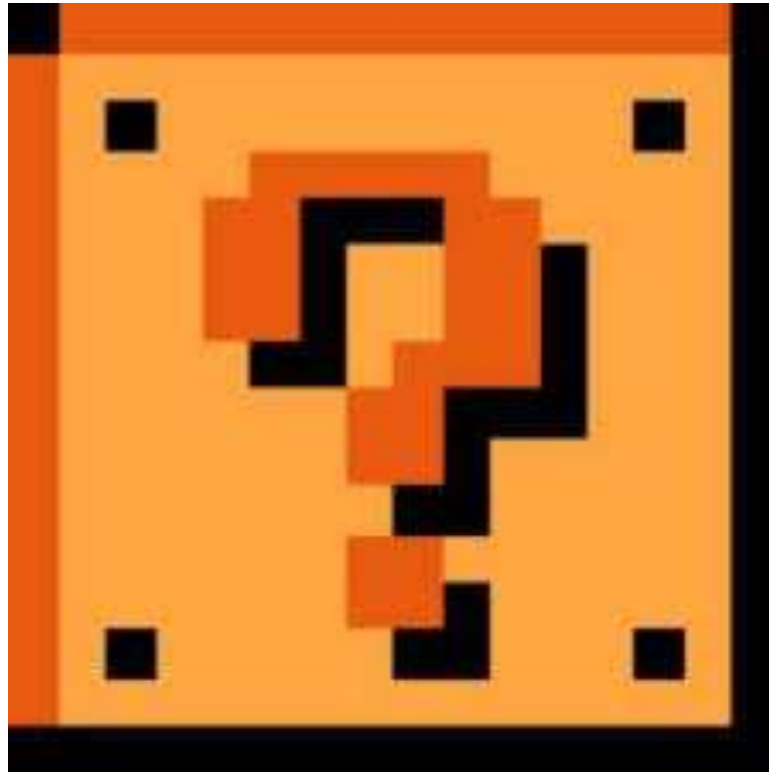










DIAGNOSIS?





Mixed Tumor of Lacrimal Gland

Epithelial Lacrimal Gland Tumors

- ▶ 4% of all Lacrimal gland lesions
- ▶ 50% Benign Mixed Tumors
- ▶ 50% Malignant (Adenoid Cystic Ca & malignancy in mixed tumors)
- ▶ Average age at Dx is 40

Key Elements of Clinical Evaluation

- ▶ Duration of symptoms
 - ▶ <6 Months, more likely to be malignant
- ▶ Pain
 - ▶ More common in malignant lesions
- ▶ Status of orbital bones on imaging
 - ▶ Bony erosion associated with malignancy

Management & Prognosis

- ▶ Tumor should be entirely excised with intact capsule
 - ▶ Recurrence in 1/3 of patients with incisional biopsy
 - ▶ No recurrences in UBC series with mean f/u of over 4 years
- ▶ Malignant transformation related to tumor age
 - ▶ 9% incidence over 15 years in literature
 - ▶ In UBC series patients with Carcinoma ex PA (CEPA) were significantly older
 - ▶ Extensive hyalinization seen in 5 of 9 CEPAs
- ▶ Arch Ophthalmol. 2009; 127(8): 1016-1028

SBPS Archives

Lacrimal Gland Lesions

- ▶ 1813 Oct 1977: ACC, Ranchod
- ▶ 3733 Mar 1995: ACC, Kohler
- ▶ 3838 Feb 1996: Sol. Fibrous Tumor, Metcalf

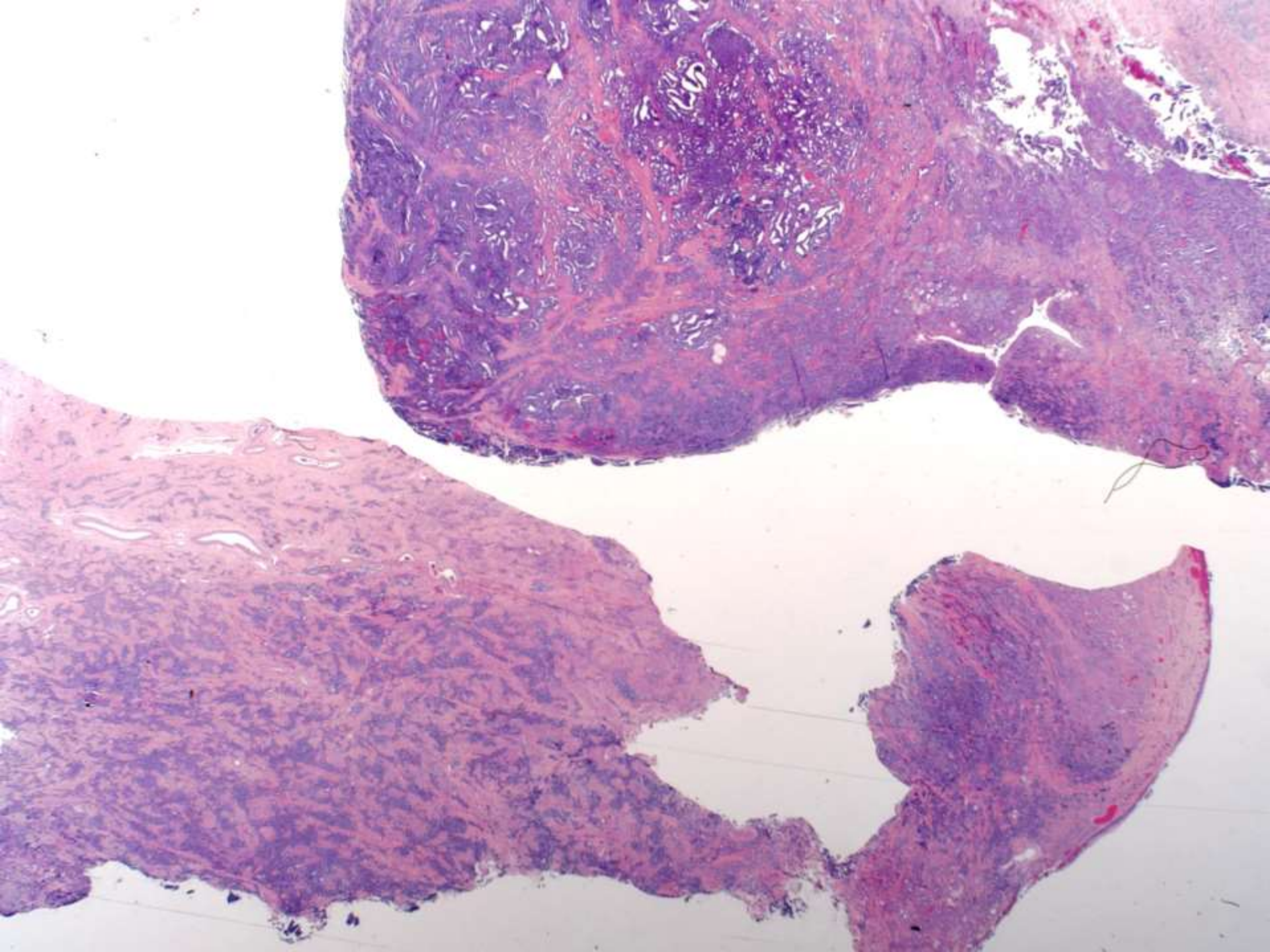
Lacrimal Gland Tumors: Take Home Points

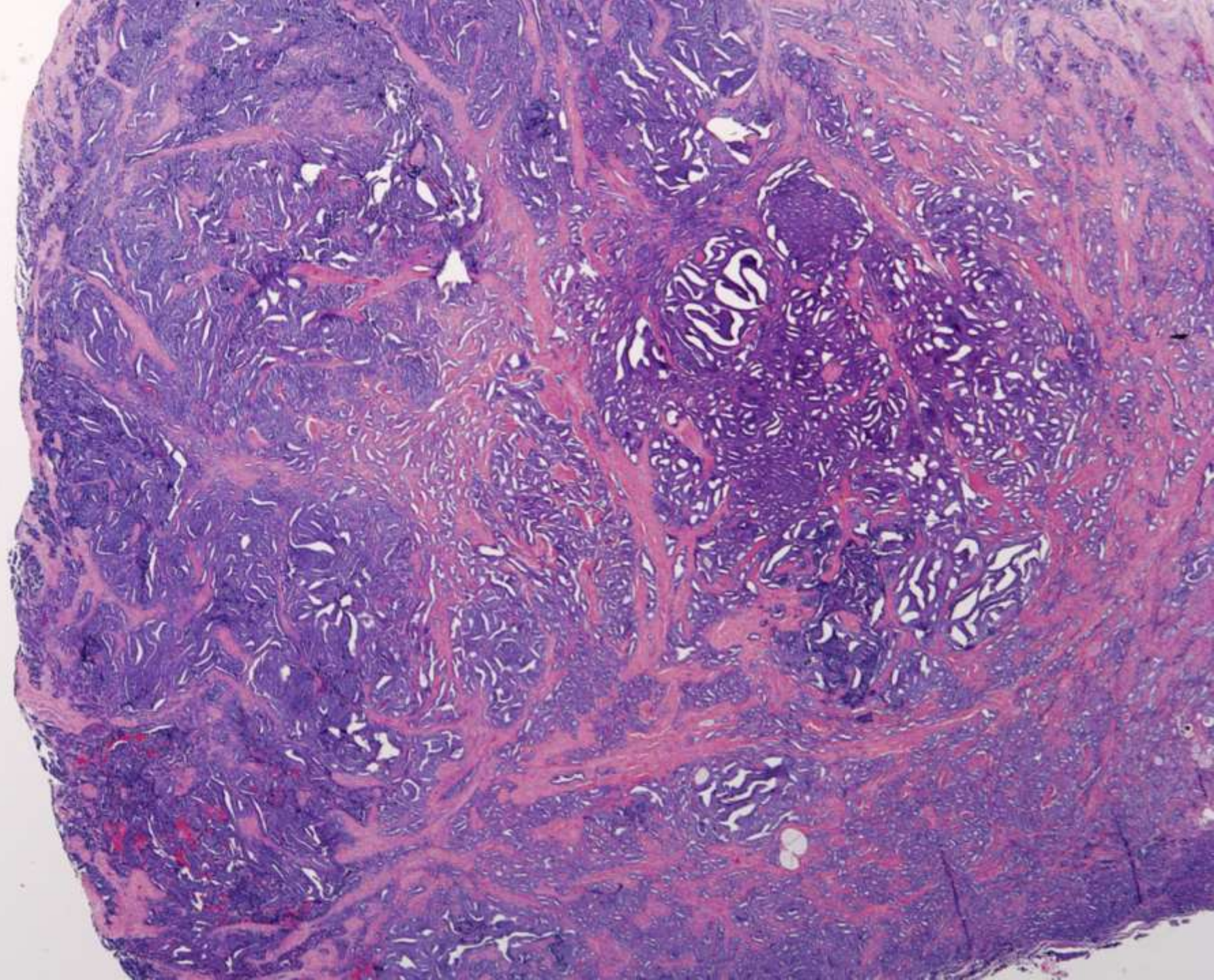
- ▶ Check clinical and radiographic findings
- ▶ 50% Mixed Tumors
- ▶ 25% Adenoid Cystic Ca
- ▶ Complete Excision

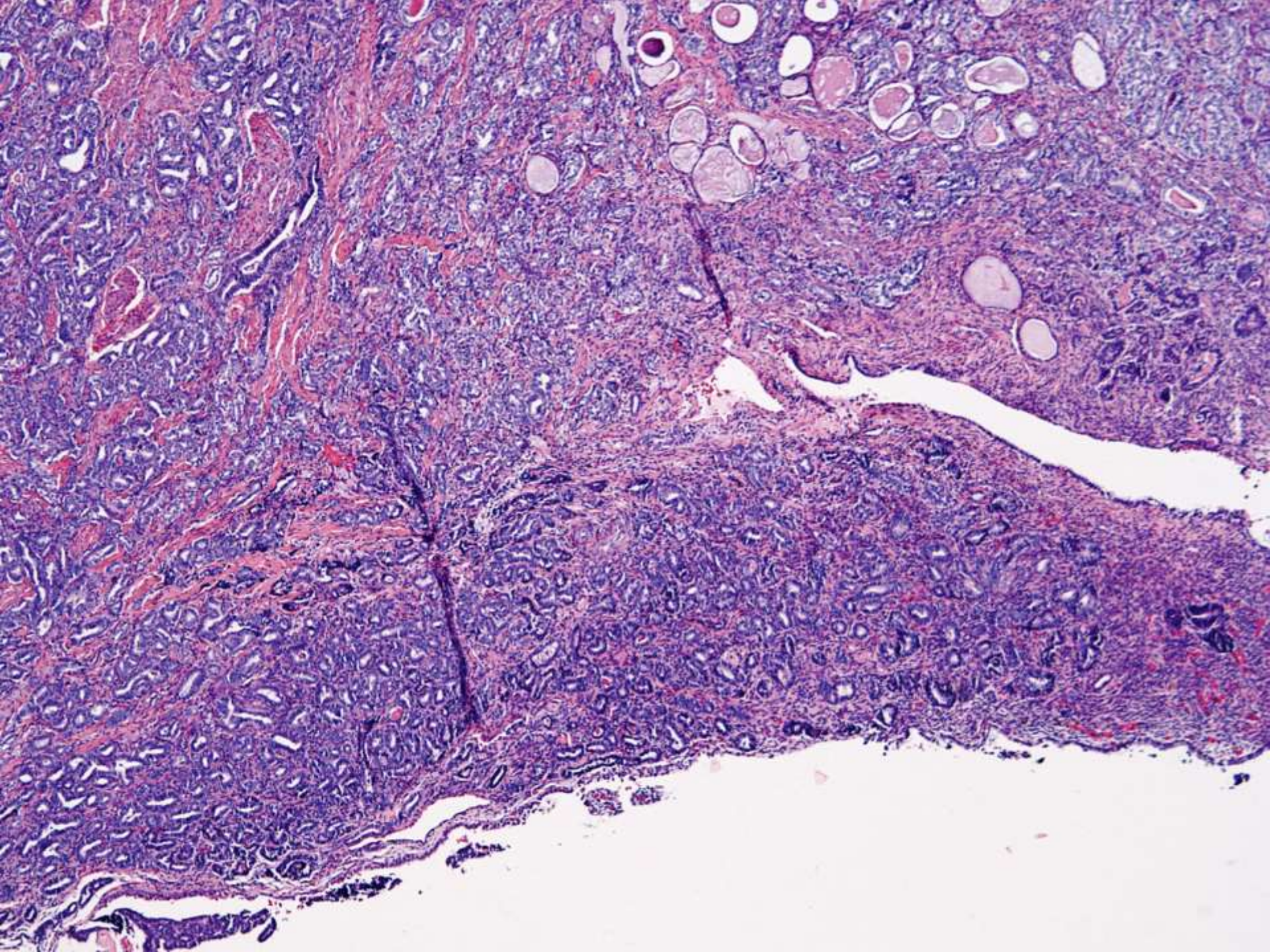
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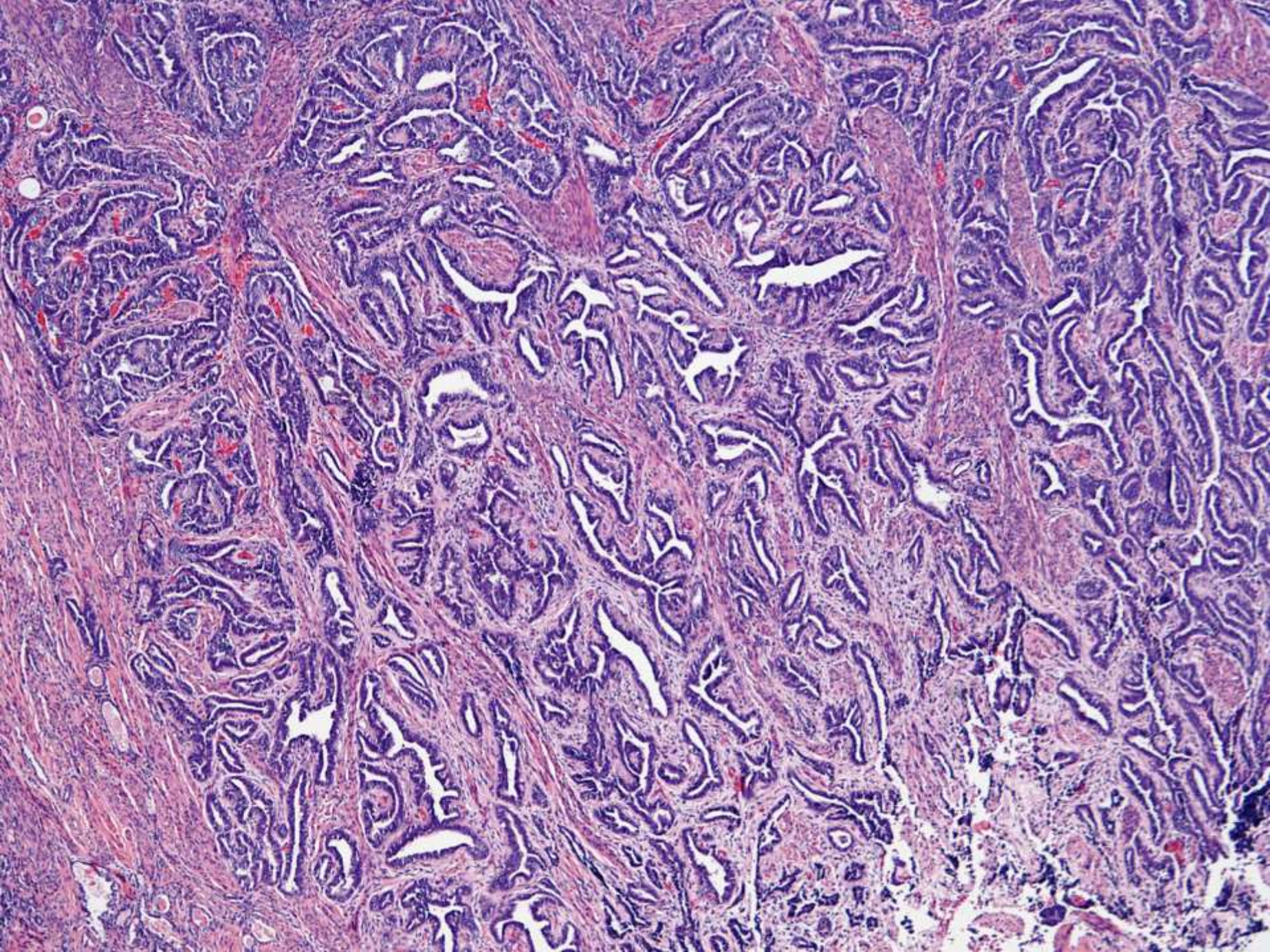
Alana Shain/Teri Longacre; Stanford

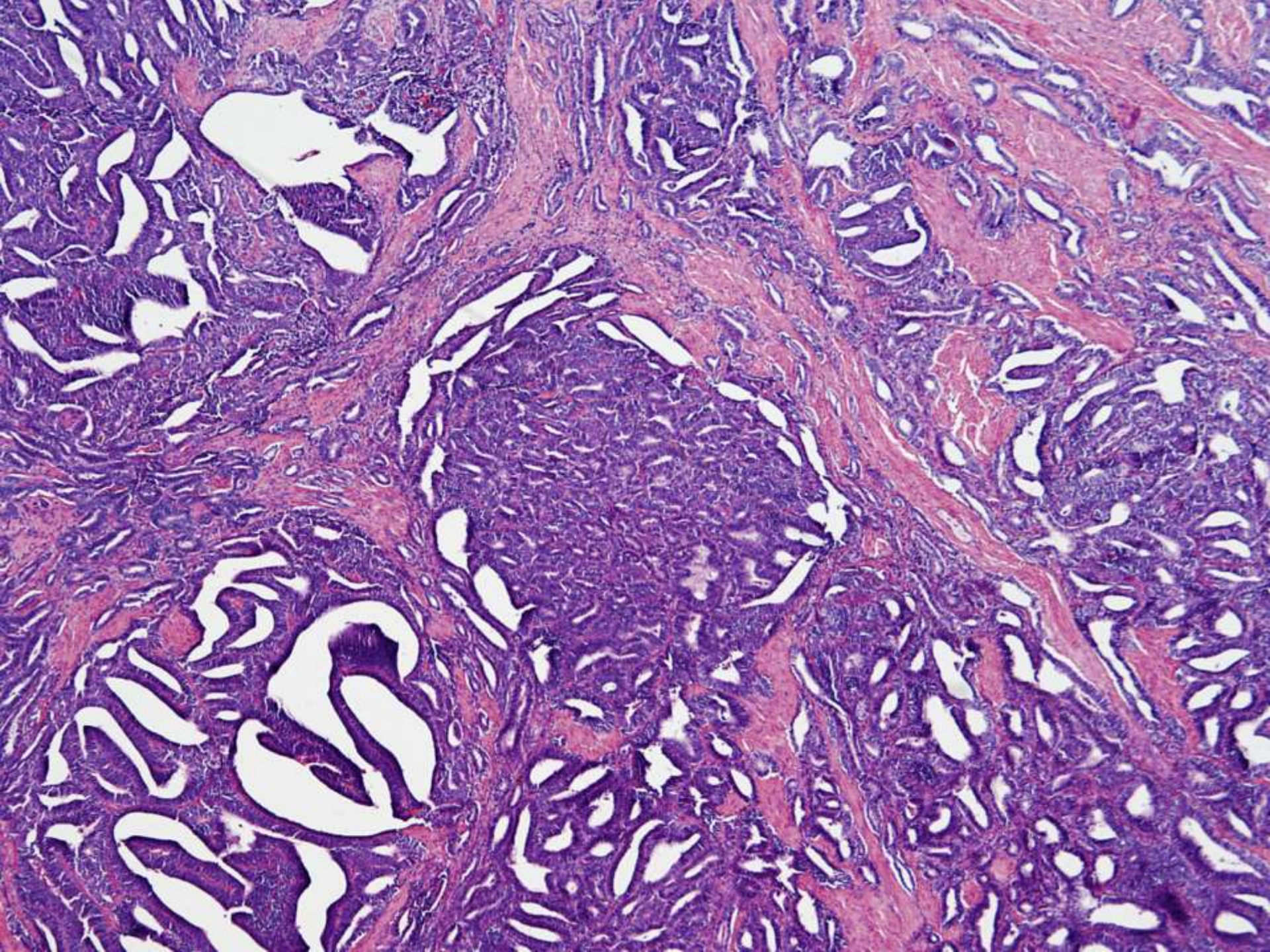
60-year-old female with complex endometrial hyperplasia.

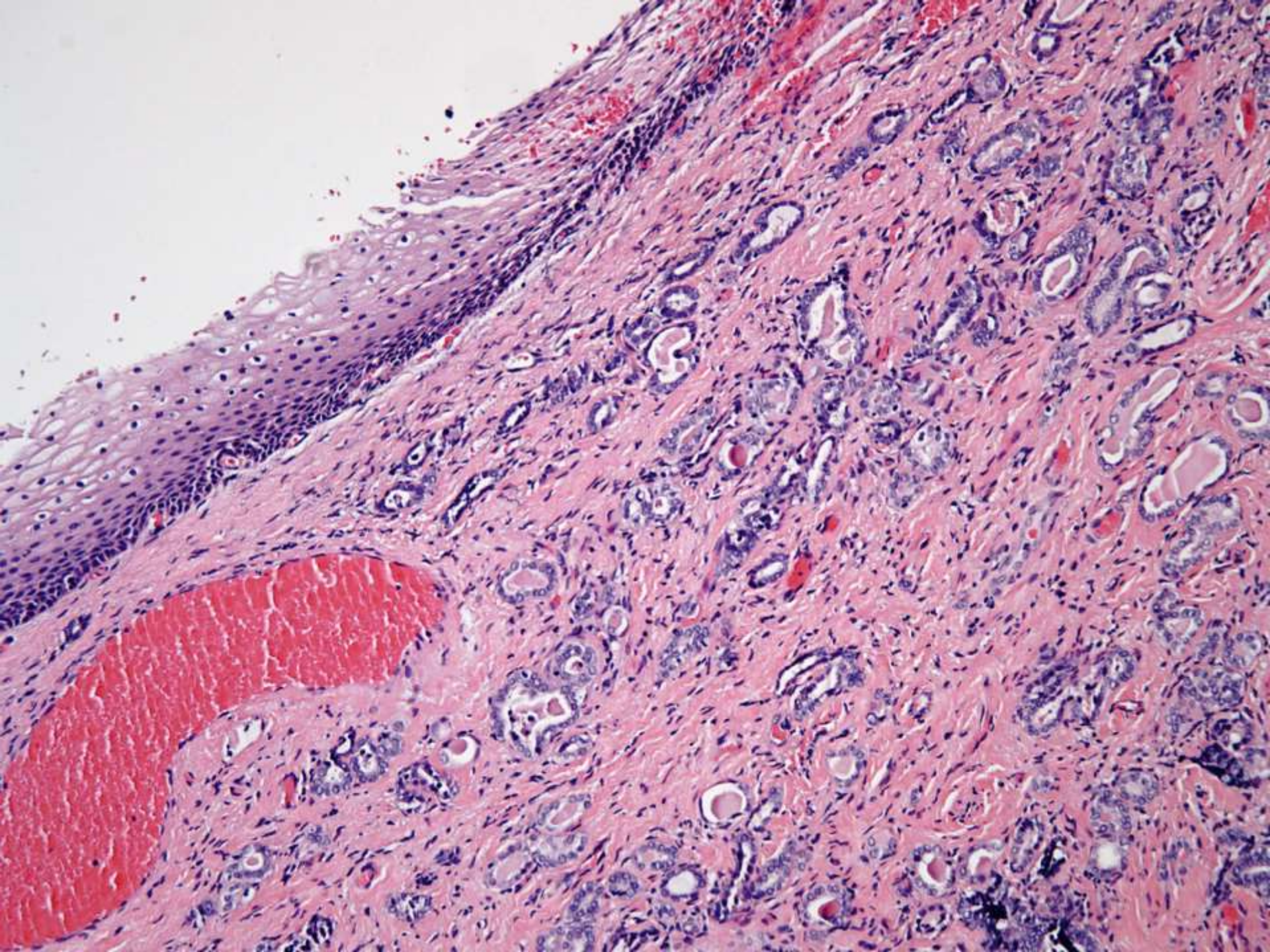


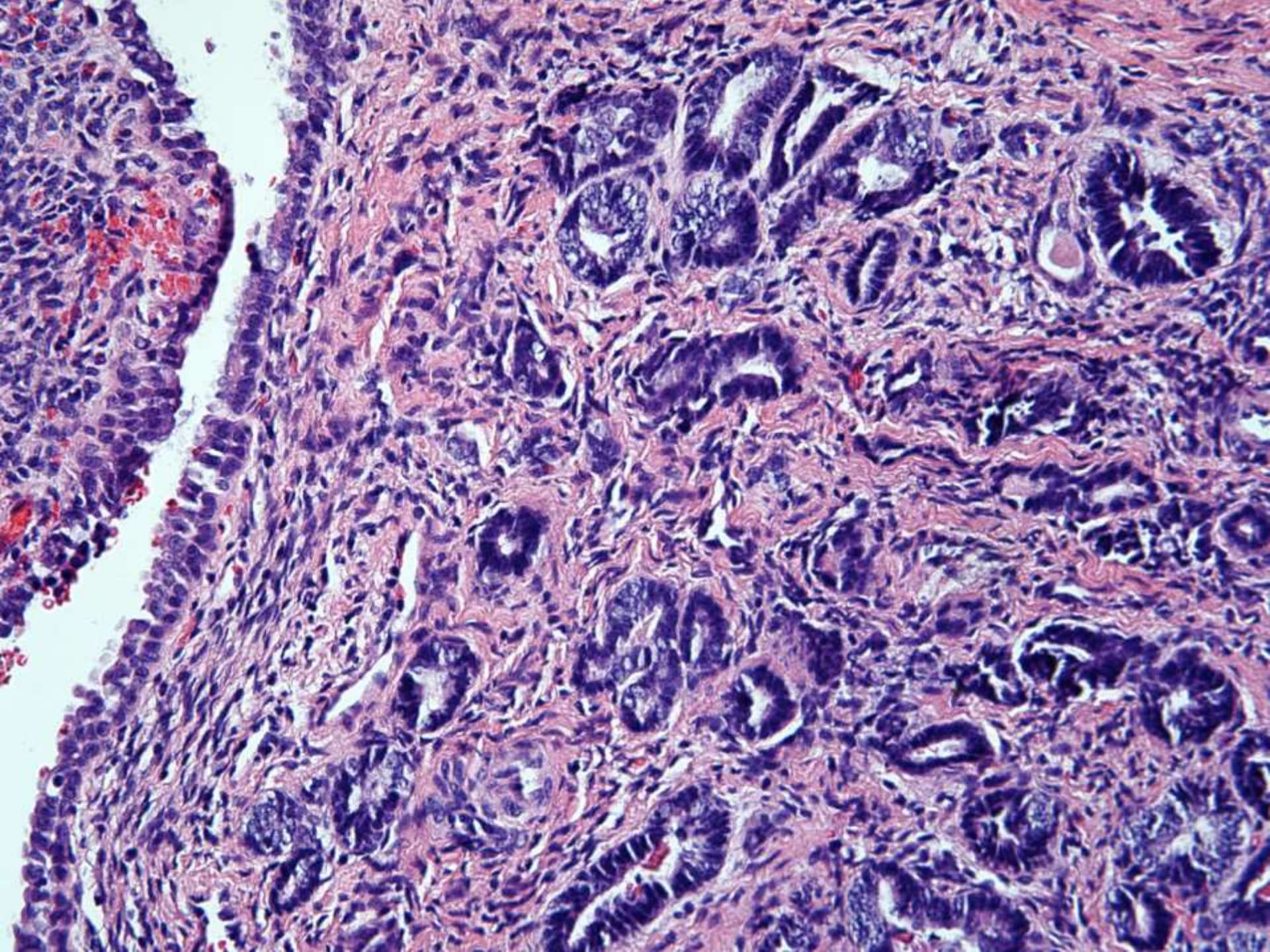


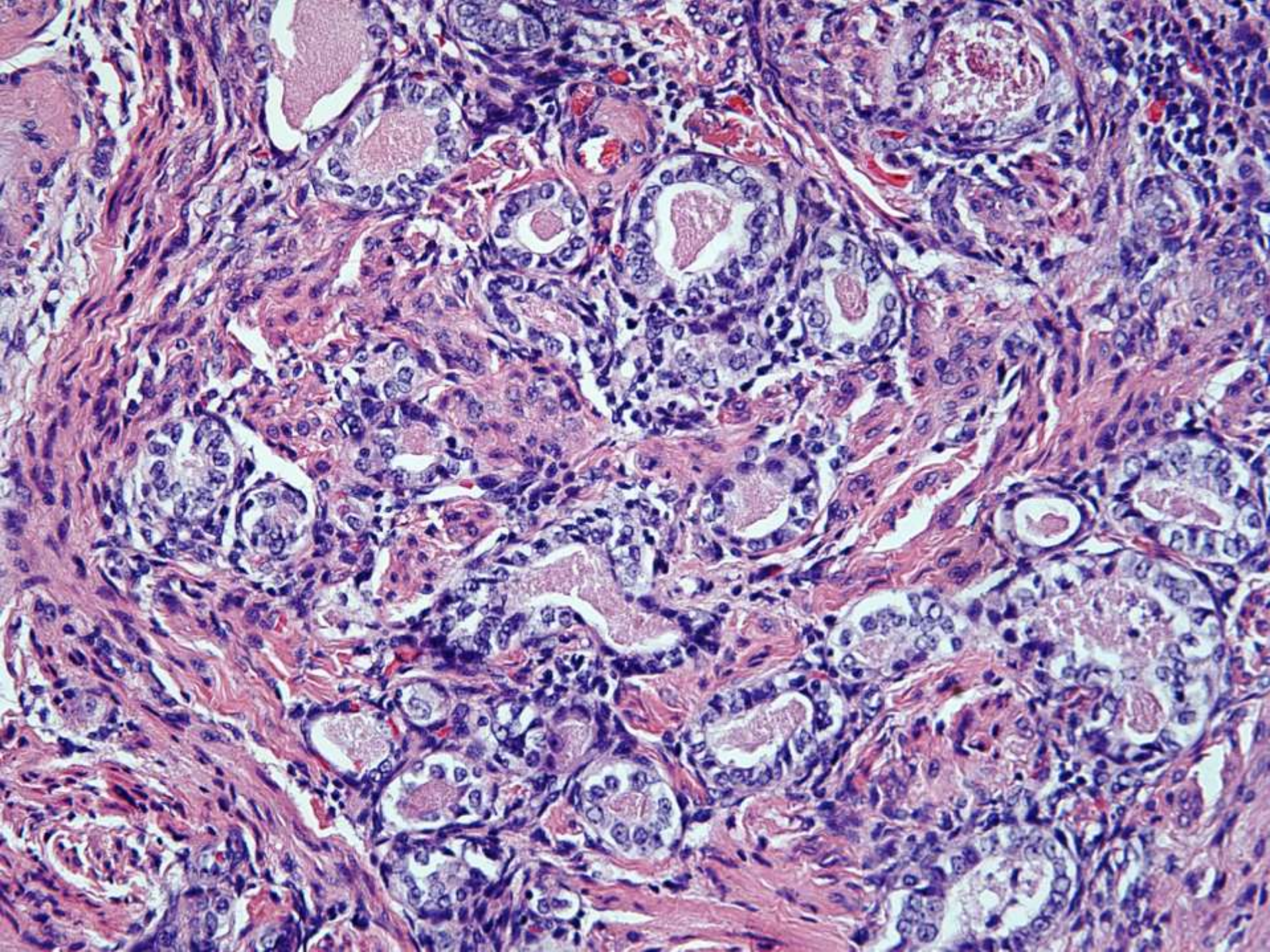


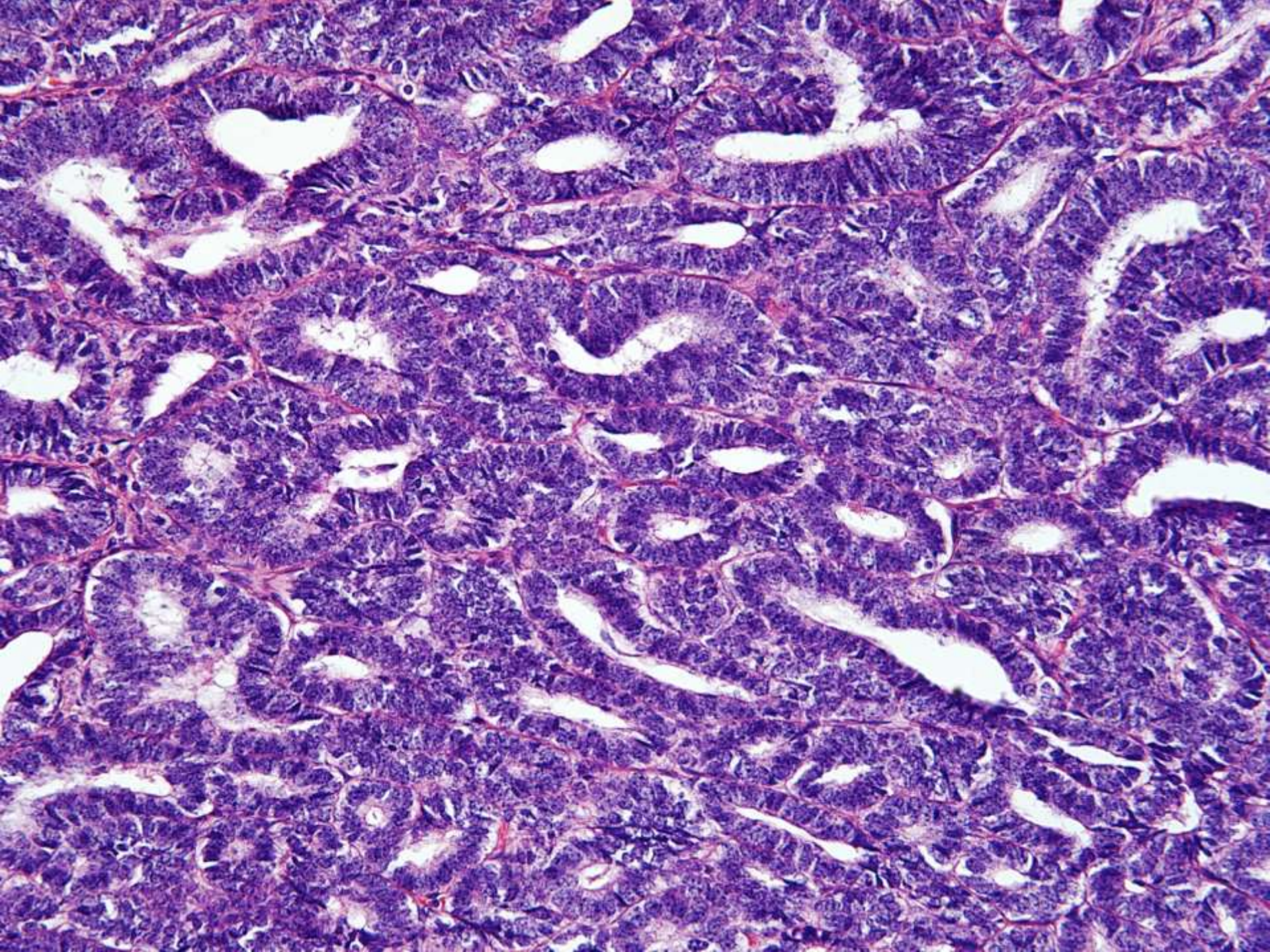




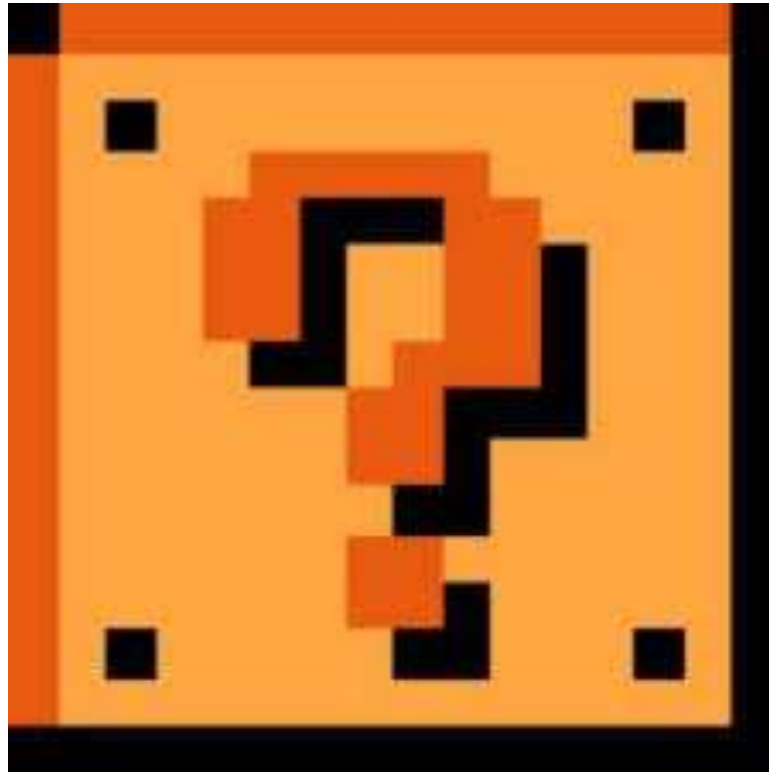








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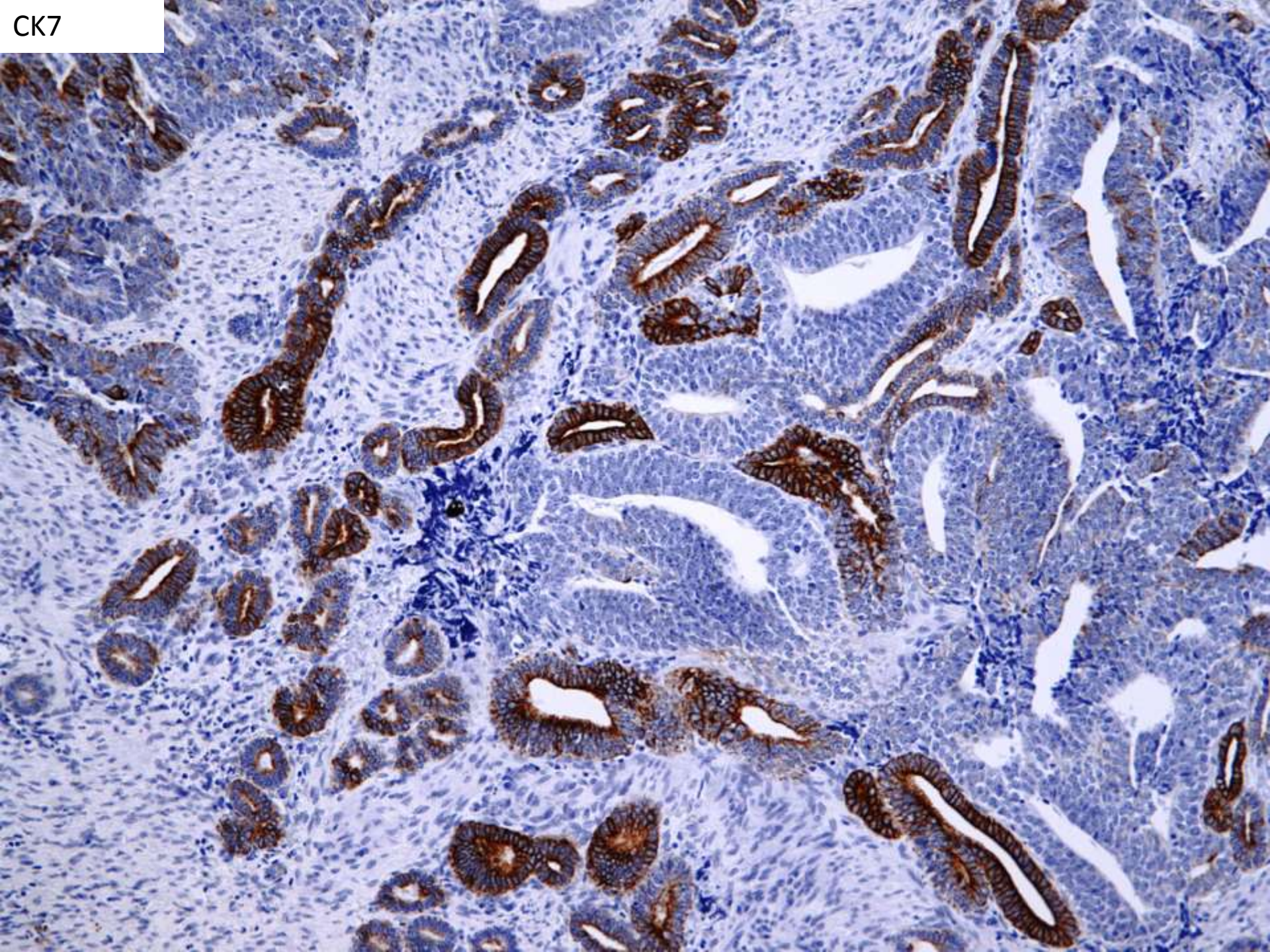


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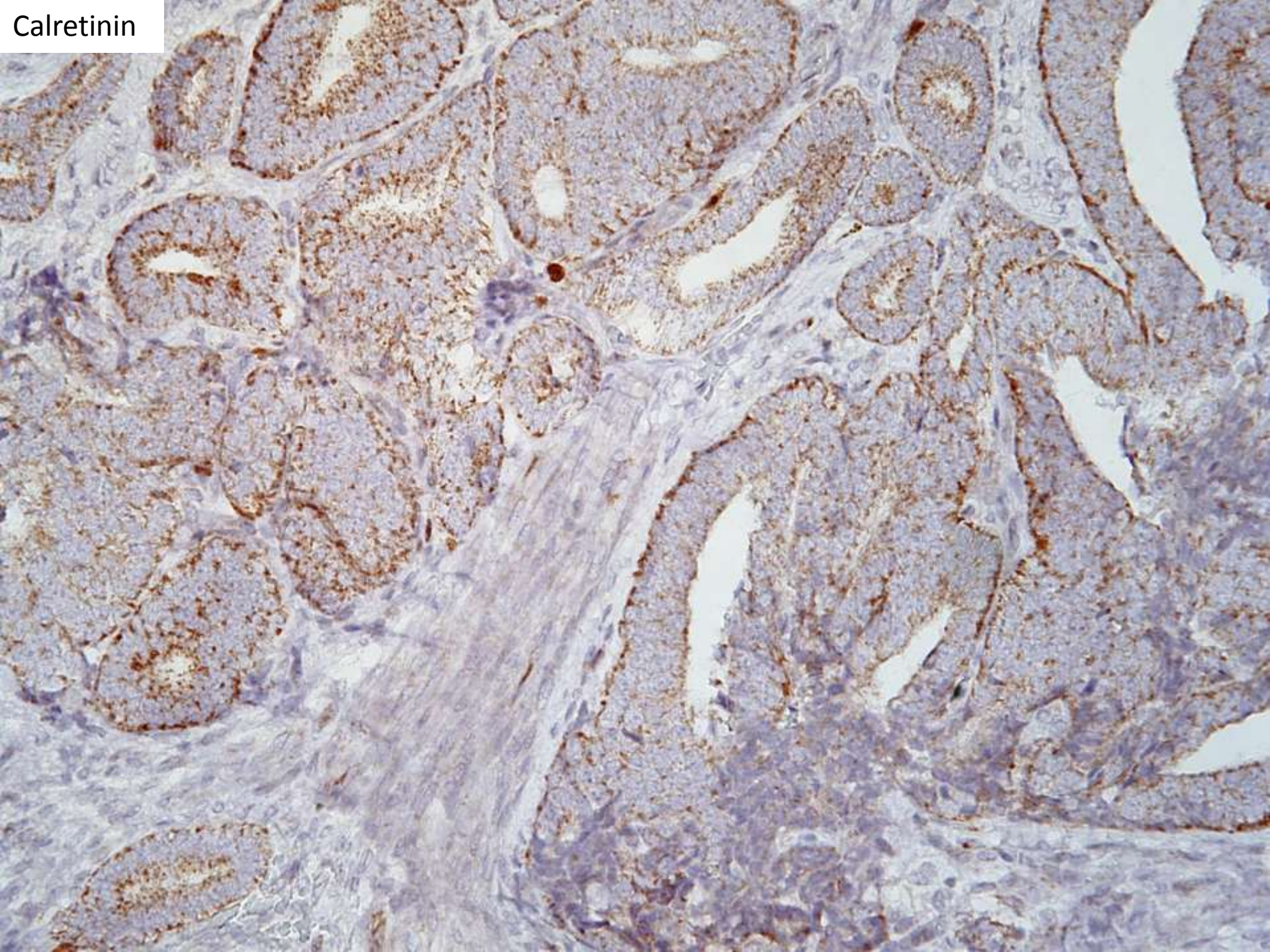
Alana Shain, MD/Teri Longacre, MD
Stanford University

Case courtesy Dr. John Pollard
(Pathology Associates, Clovis, CA)

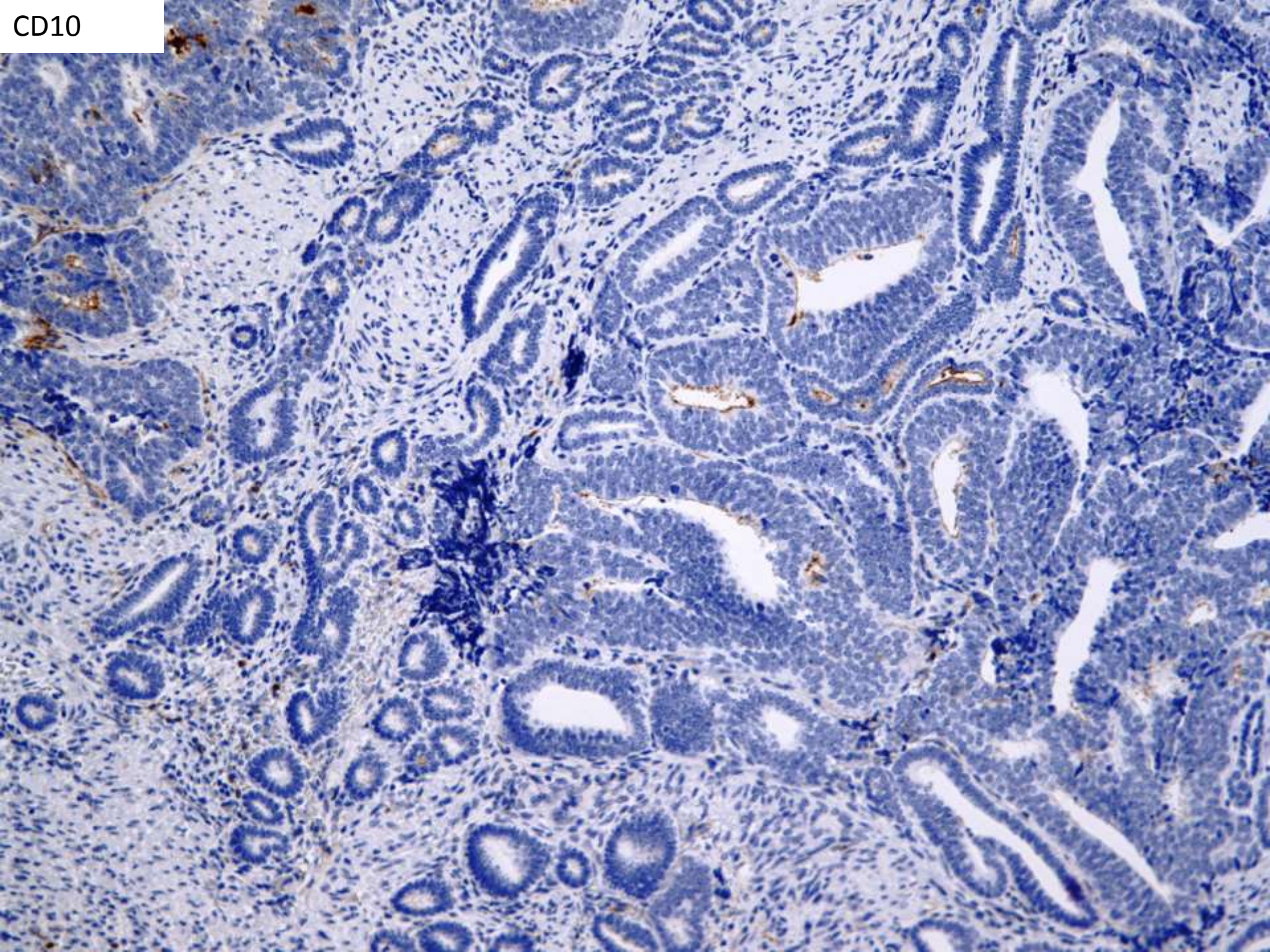
CK7



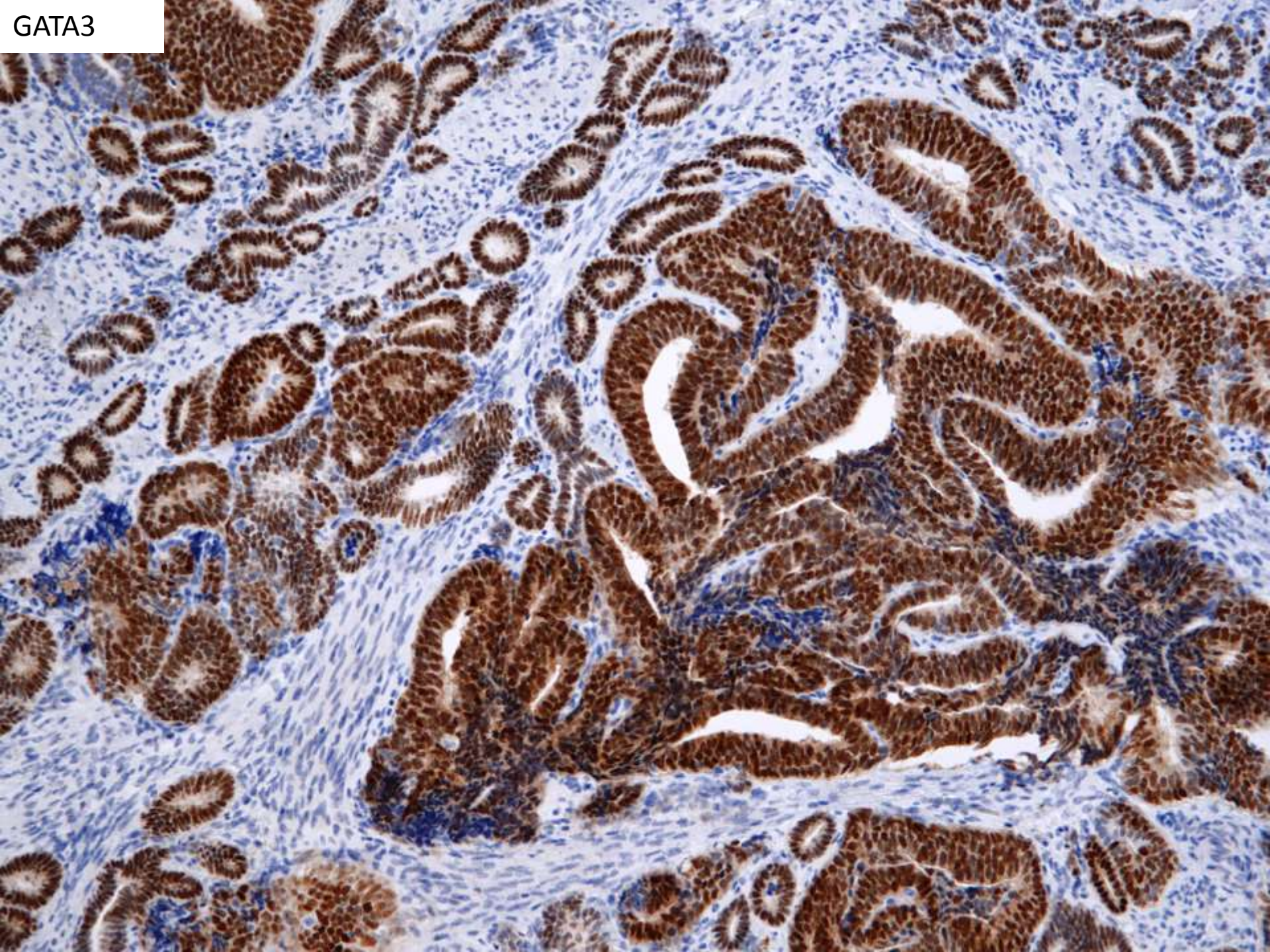
Calretinin



CD10



GATA3



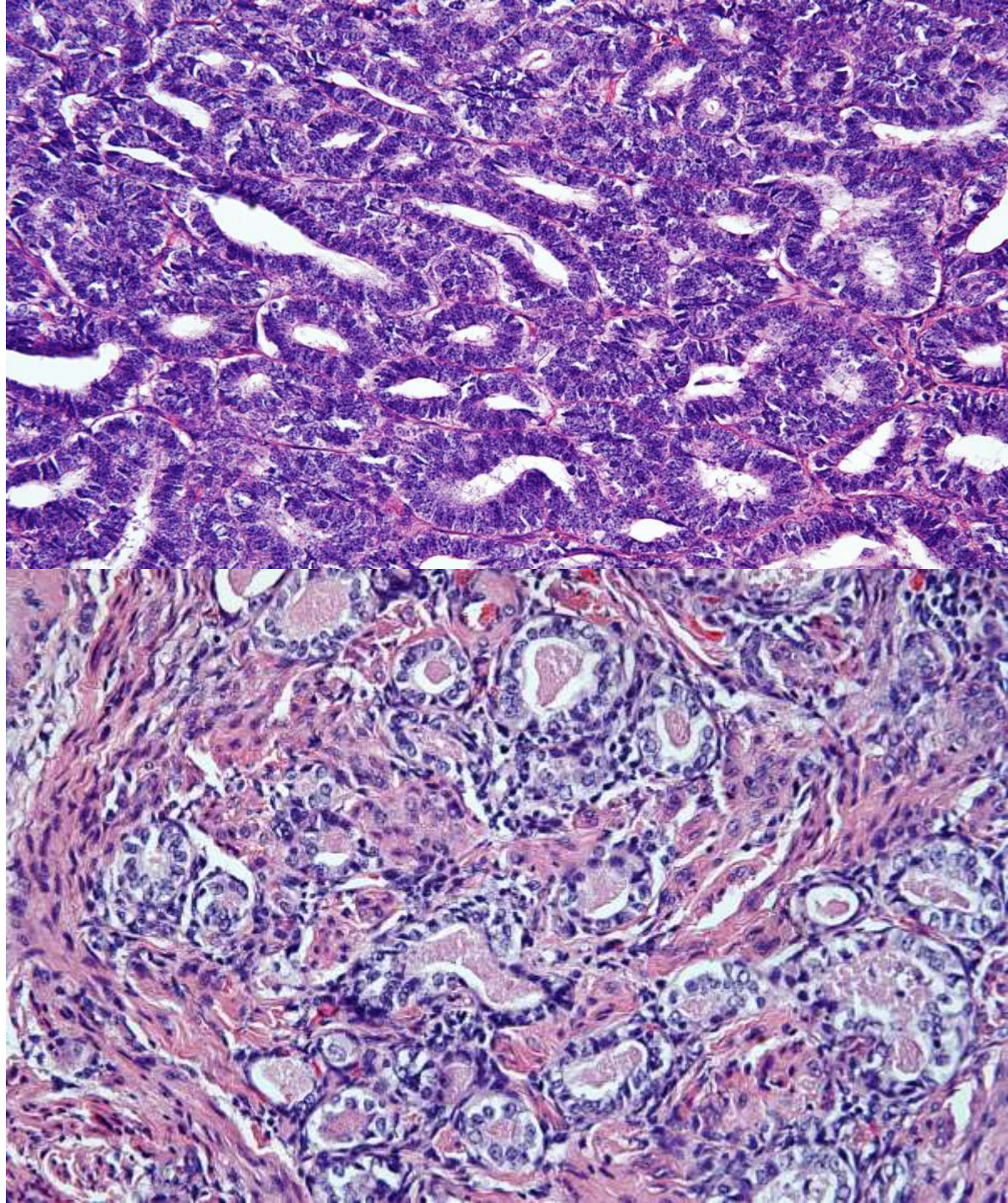
Summary

Positive

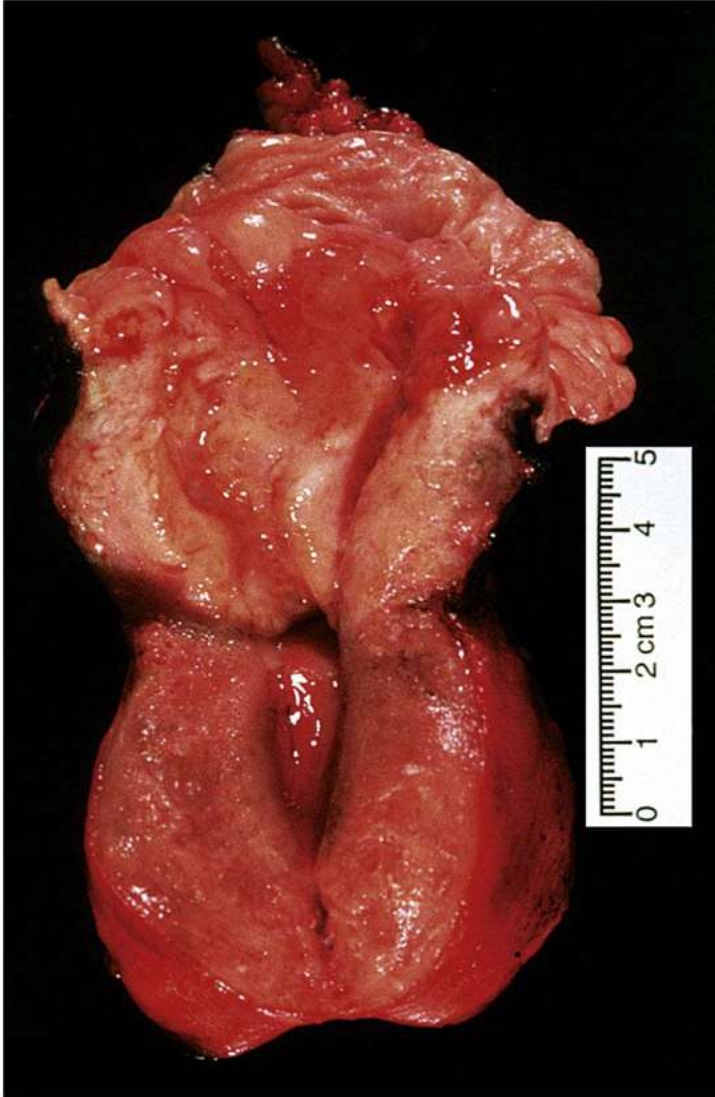
- CK7
- Calretinin
- Vimentin (focal)
- GATA-3

Negative

- ER, PR
- CEA
- p16
- P63
- CD10



Mesonephric adenocarcinoma



Clinical

Early 50s

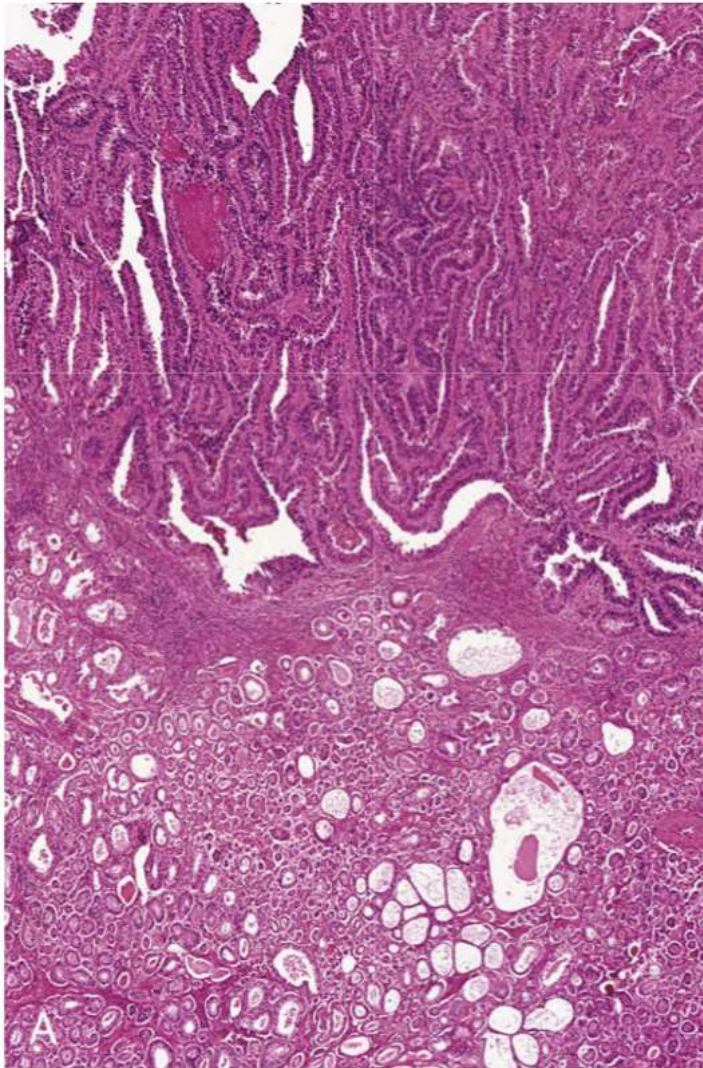
Abnormal vaginal bleeding

Gross

Wall of cervix → LUS

Bulky, deeply invasive

Mesonephric adenocarcinoma



Micro

Glandlike spaces

Intraluminal eosinophilic
hyaline secretions

Variable patterns

- Tubular or Ductal
(most frequent)
- Retiform
- Papillary
- Solid
- Spindle cell
- Sex-cord like

Differential Diagnosis

Florid mesonephric hyperplasia	No symptomatic mass (incidental finding) Non-infiltrative pattern Uniform glands
Endocervical adenocarcinoma	HPV driven (p16)
Endometrioid adenocarcinoma	Location (typically involve cervical surface) Higher-grade nuclear atypia ER+/PR+
Clear cell, Serous carcinomas	Higher-grade nuclear atypia
UTROSCT	Predominant spindle cell component with minor tubule forming component

Immunohistochemistry

Positive

CK7

EMA

Vimentin

Calretinin

[CD10]

GATA3

Negative

CK20

mCEA

ER

PR

WT1

GATA3

- Mesonephric lesions in the lower genital tract
- Benign *and* malignant
- Sensitivity 97.87%, Specificity 98.04%

20/21 (95%) mesonephric carcinomas
3/162 (2%) endometrial adenocarcinoma
1/30 (3%) usual-type endocervical adenocarcinoma

Our Patient

Presented with post-menopausal bleeding

- Total hysterectomy and BSO
- Received chemotherapy and radiation

Disease **progression**

- Imaging shows multiple lung and liver lesions

Plan: Treatment recommendations based on treatment of recurrent endometrial cancer

References

Diagnostic Gynecologic and Obstetric Pathology, 2nd ed. Crum, Nucci, Lee.

Howitt B E, Emori M, Drapkin R, Gaspar C, Barletta J A, Nucci M R, McCluggage W G, Oliva E, Hirsch M S. 2015. GATA3 Is a Sensitive and Specific Marker of Benign and Malignant Mesonephric Lesions in the Lower Female Genital Tract. The American journal of surgical pathology 39 (10): 1411-1419.

Ordi J, Nogales F F, Palacin A, Márquez M, Pahisa J, Vanrell J A, Cardesa A. 2001. Mesonephric adenocarcinoma of the uterine corpus: CD10 expression as evidence of mesonephric differentiation. The American journal of surgical pathology 25 (12): 1540-1545.

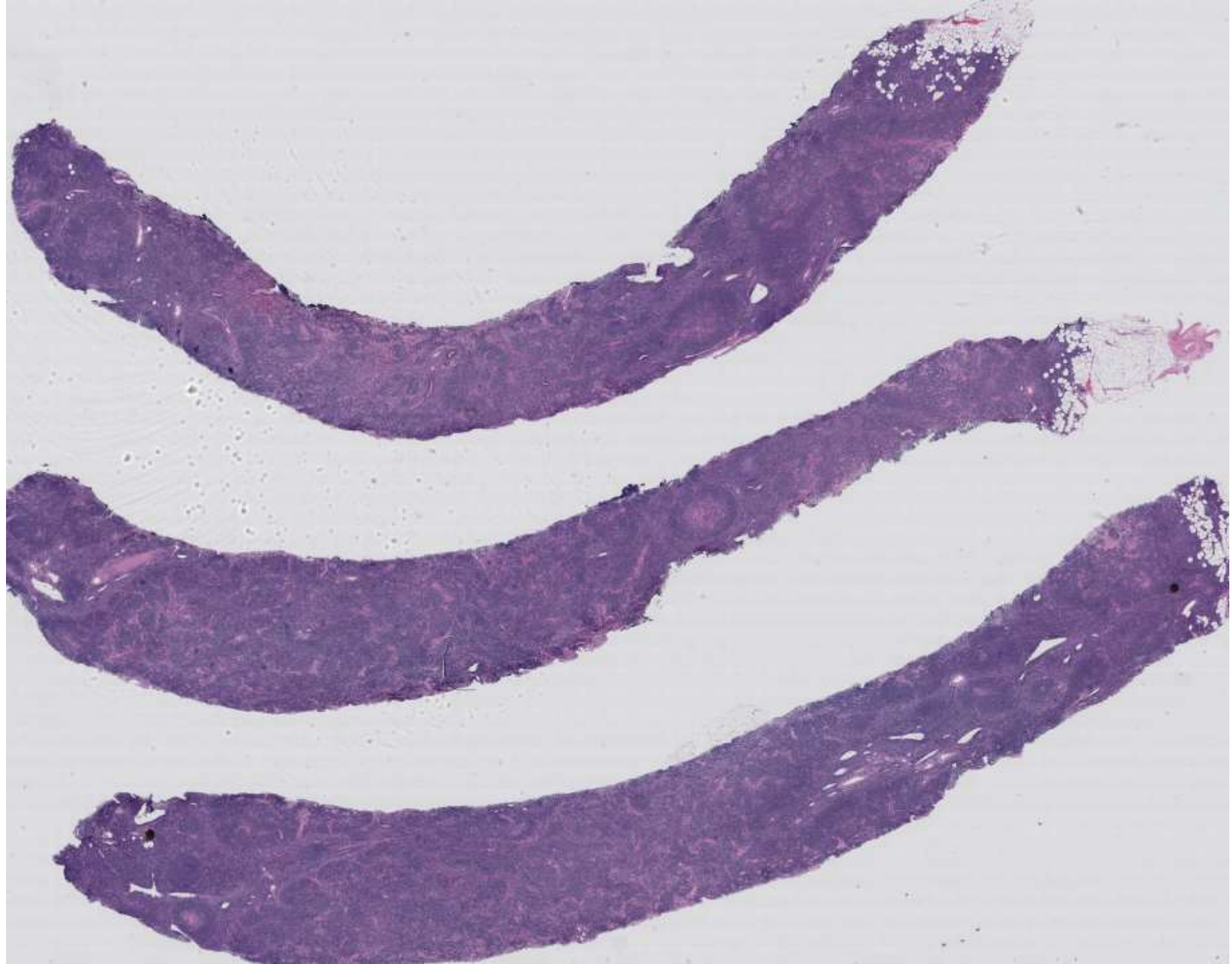
Silver S A, Devouassoux-Shisheboran M, Mezzetti T P, Tavassoli F A. 2001. Mesonephric adenocarcinomas of the uterine cervix: a study of 11 cases with immunohistochemical findings. The American journal of surgical pathology 25 (3): 379-387.

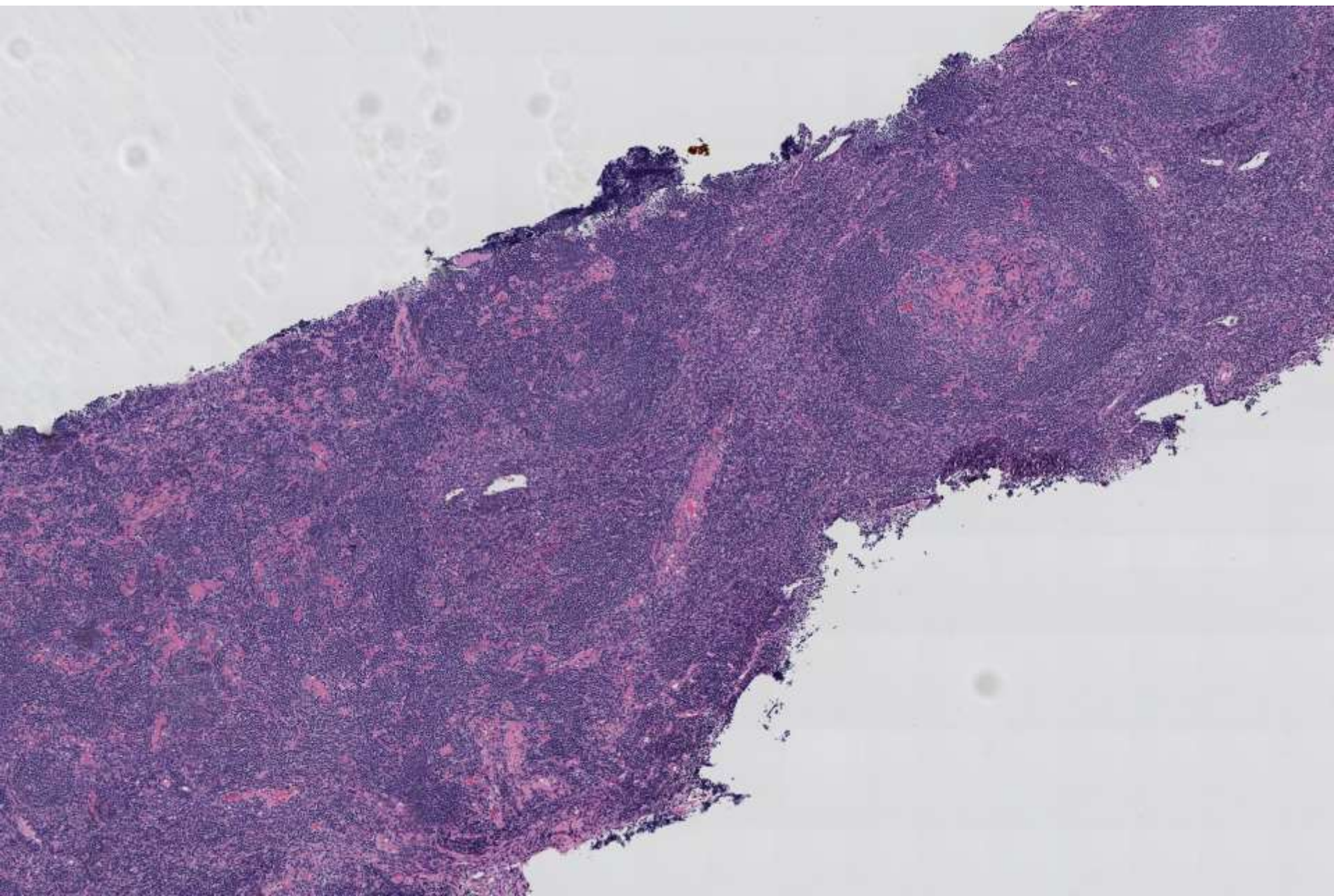
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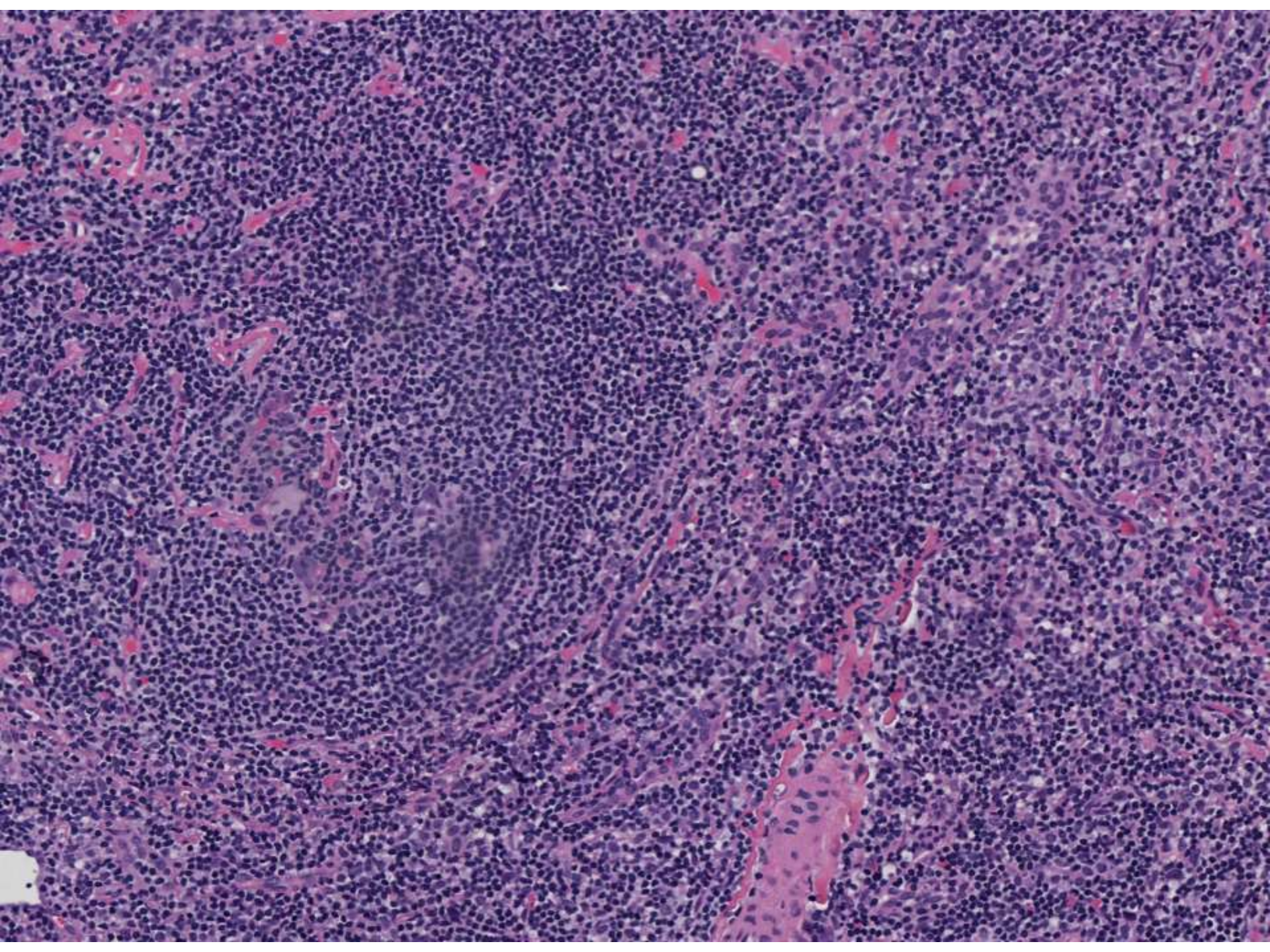
Eugene Carneal/Yaso Natkunam; Stanford

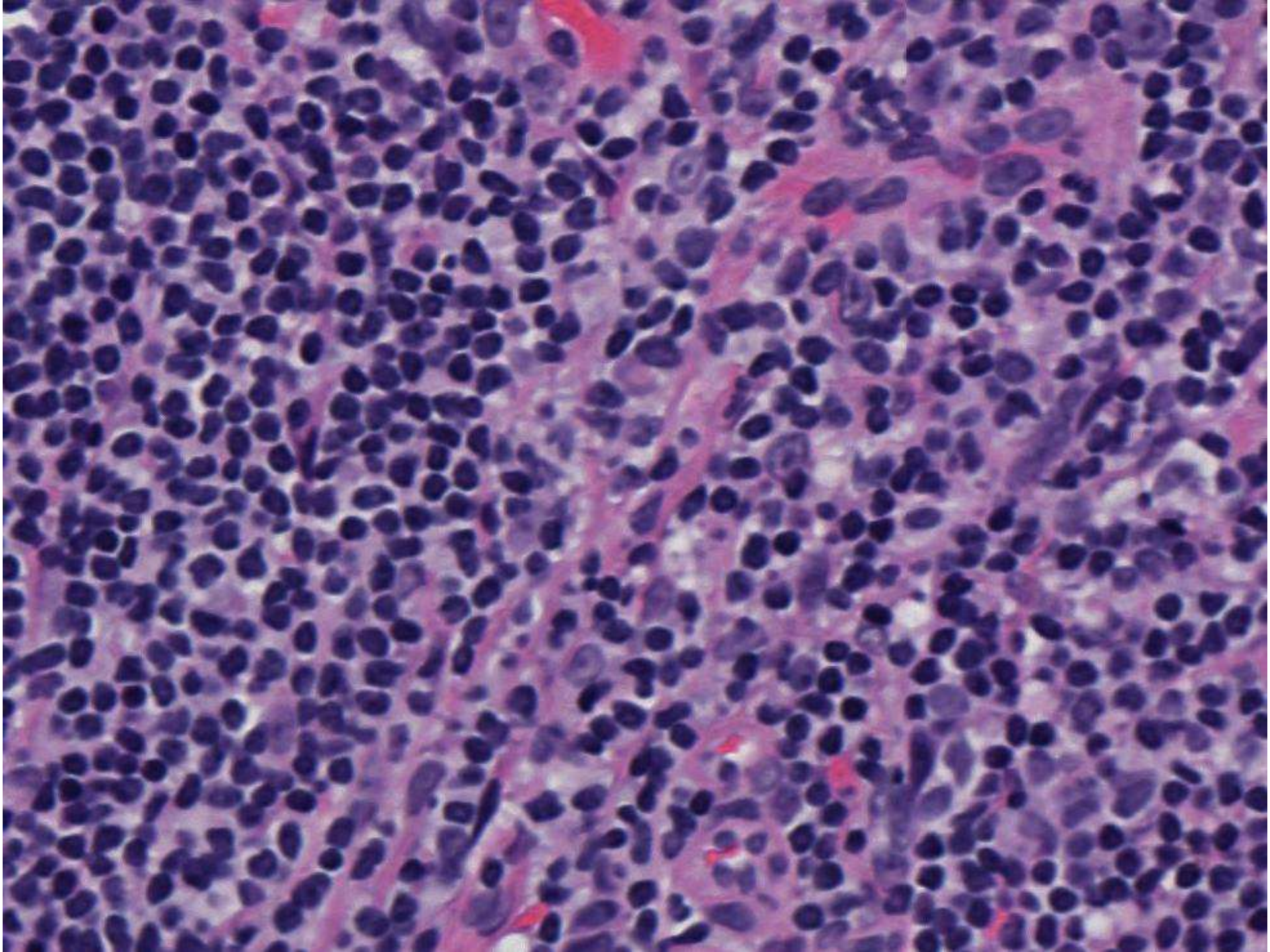
36-year-old female with enlarged right axillary lymph node.

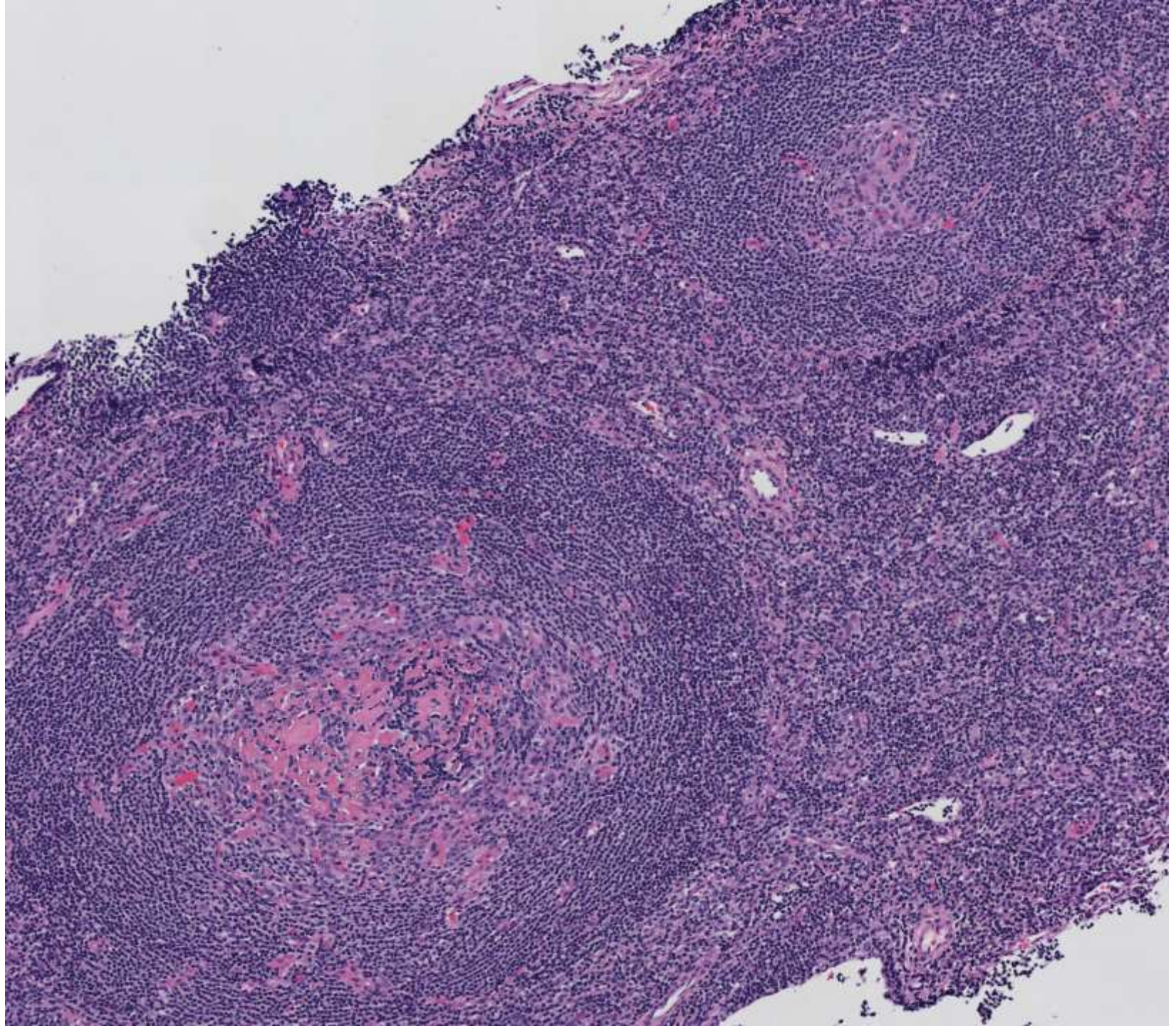
“Rule out metastatic cancer versus reactive node”.

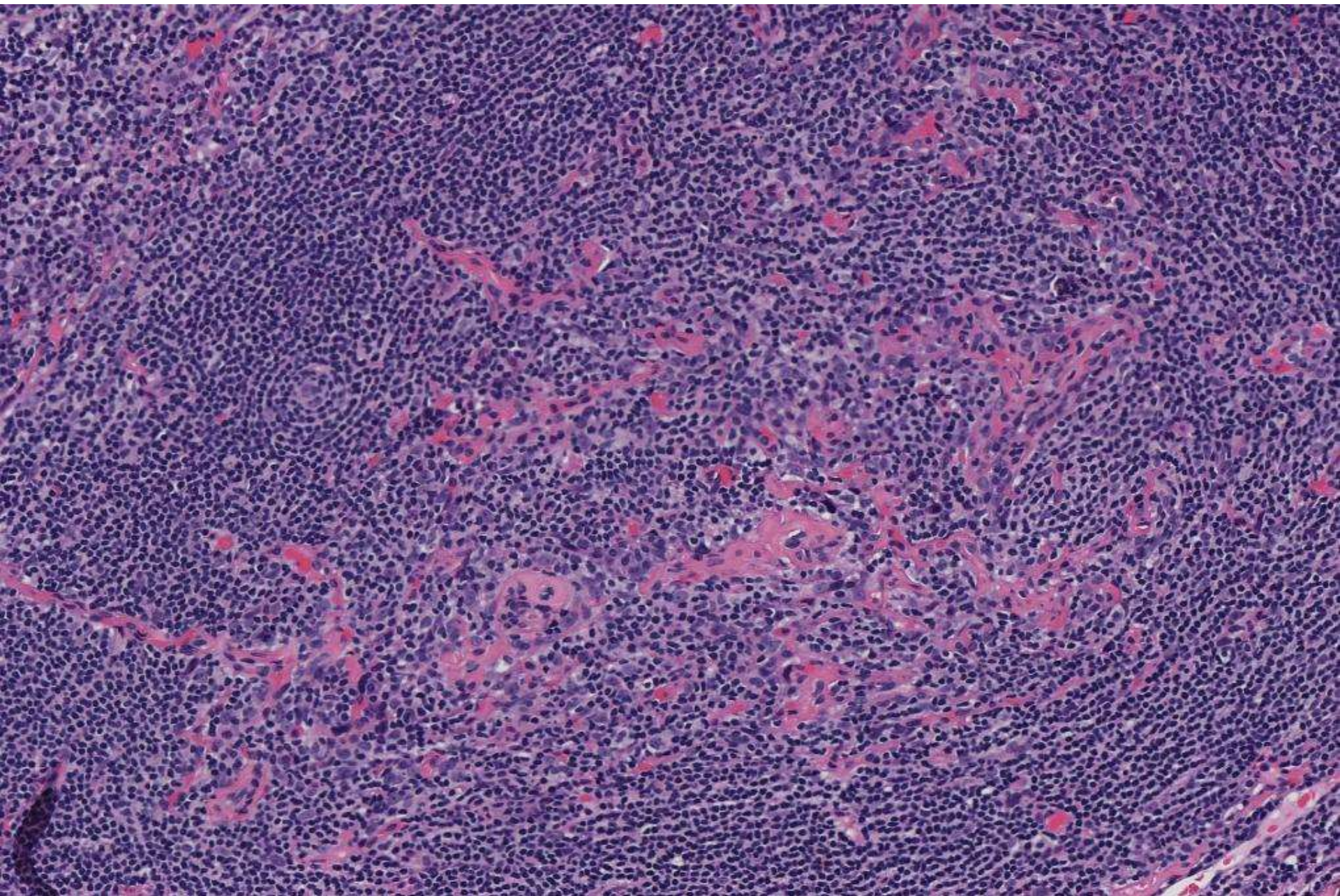


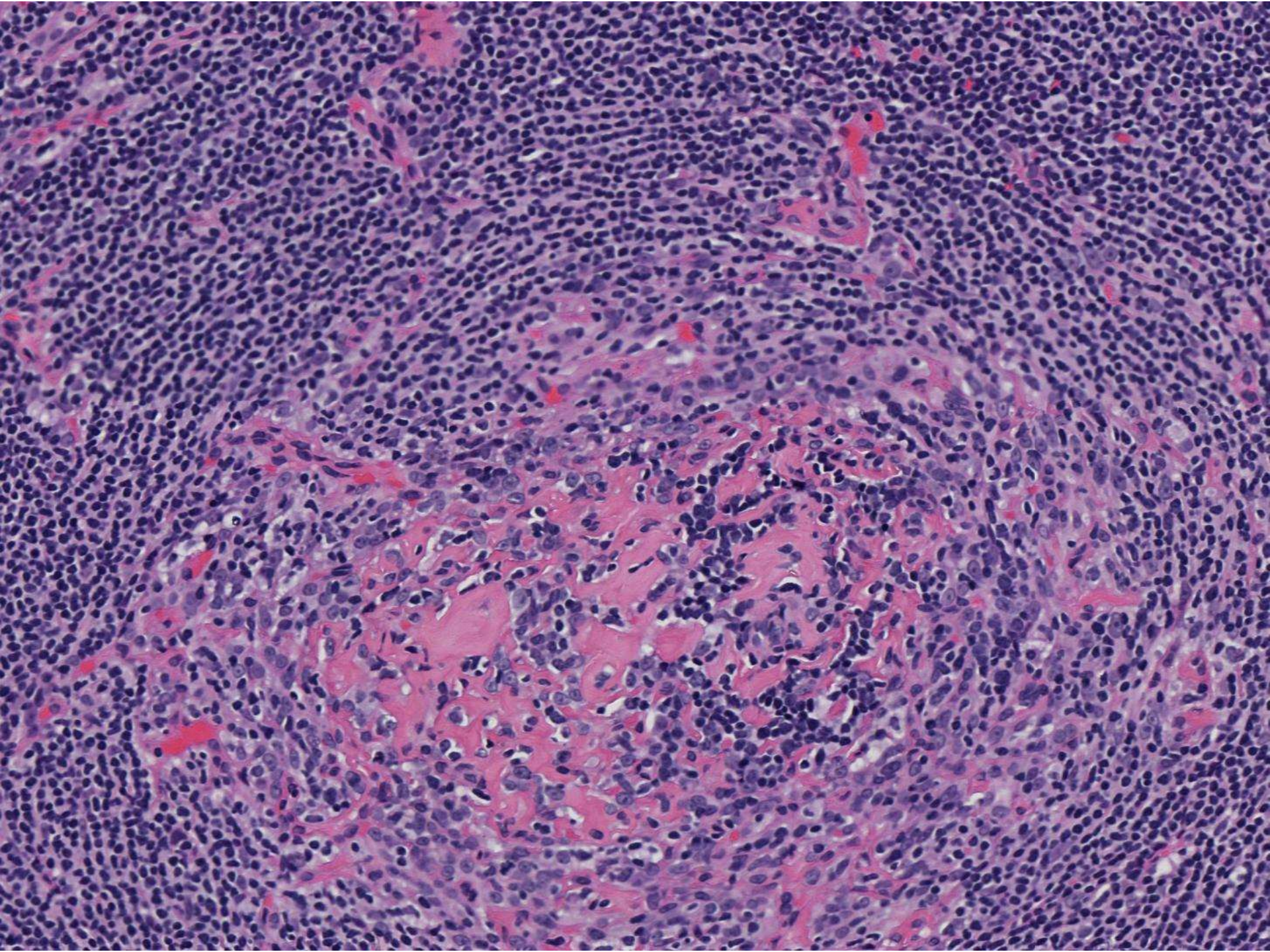


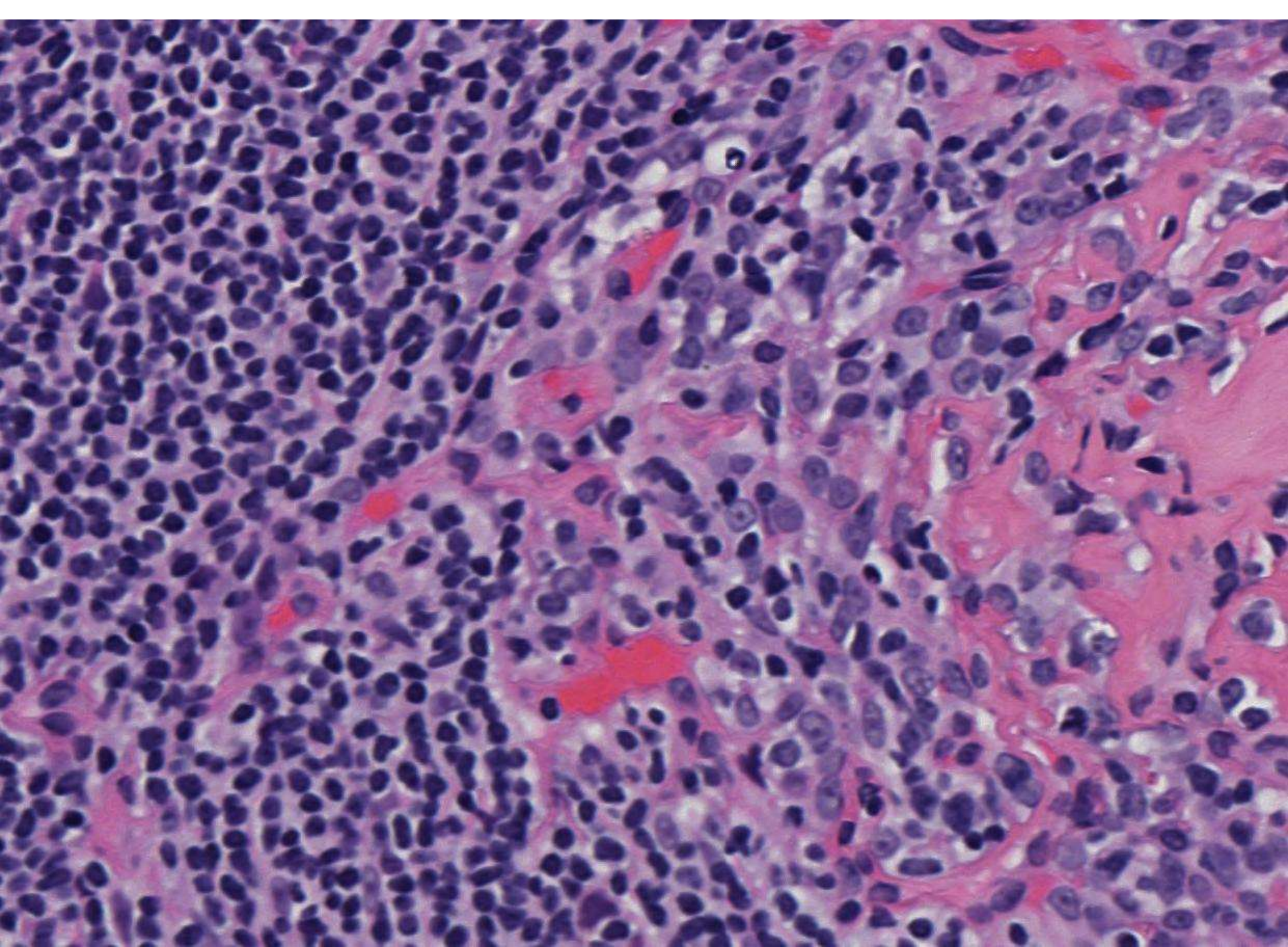




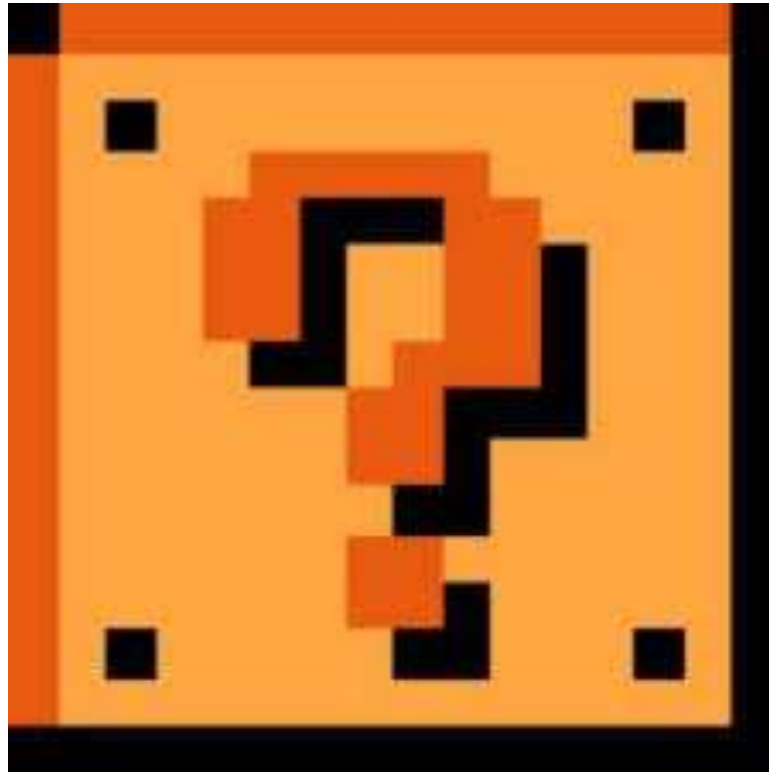




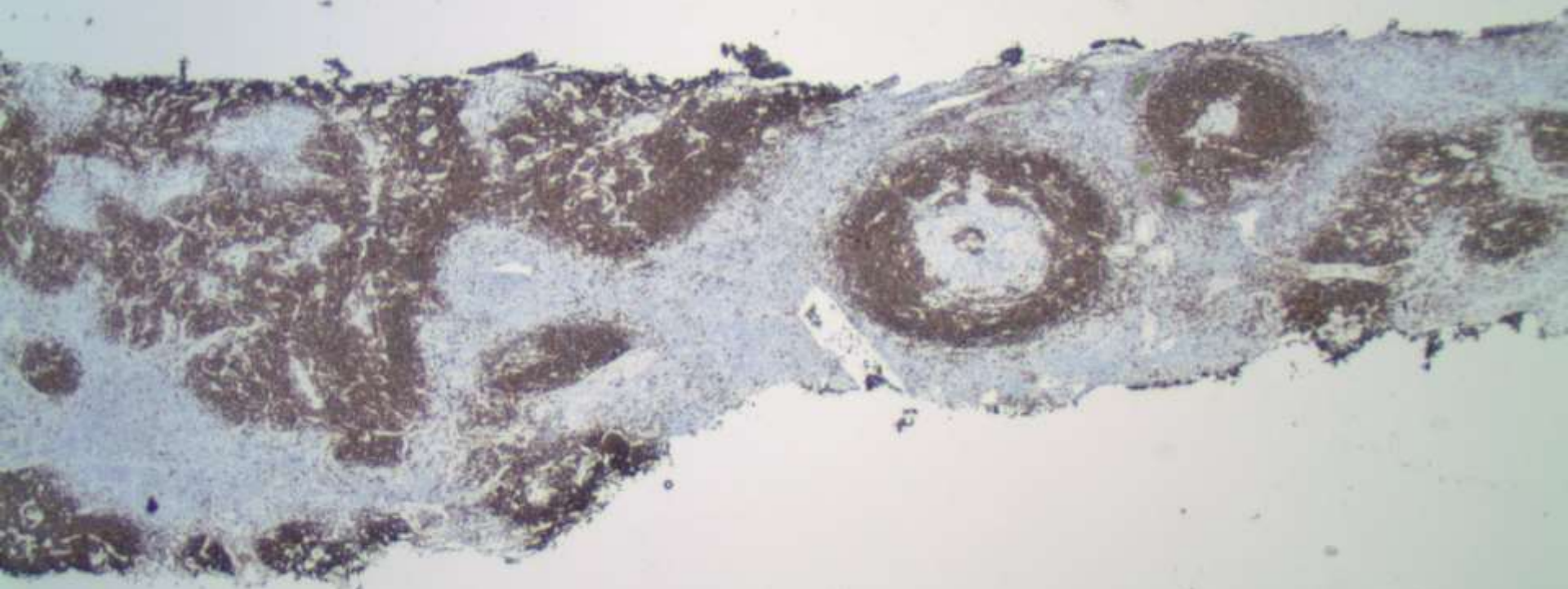




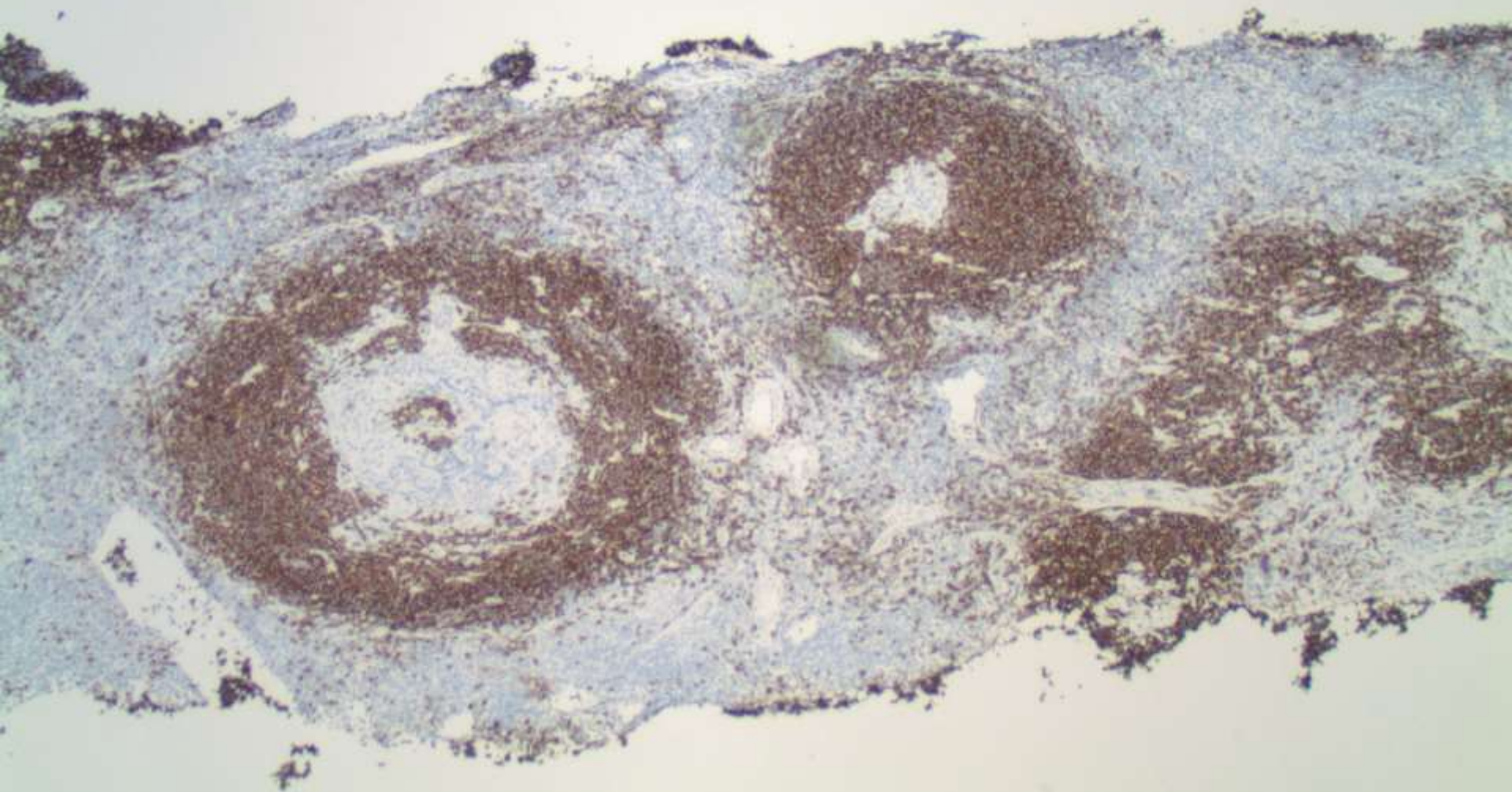
DIAGNOSIS?



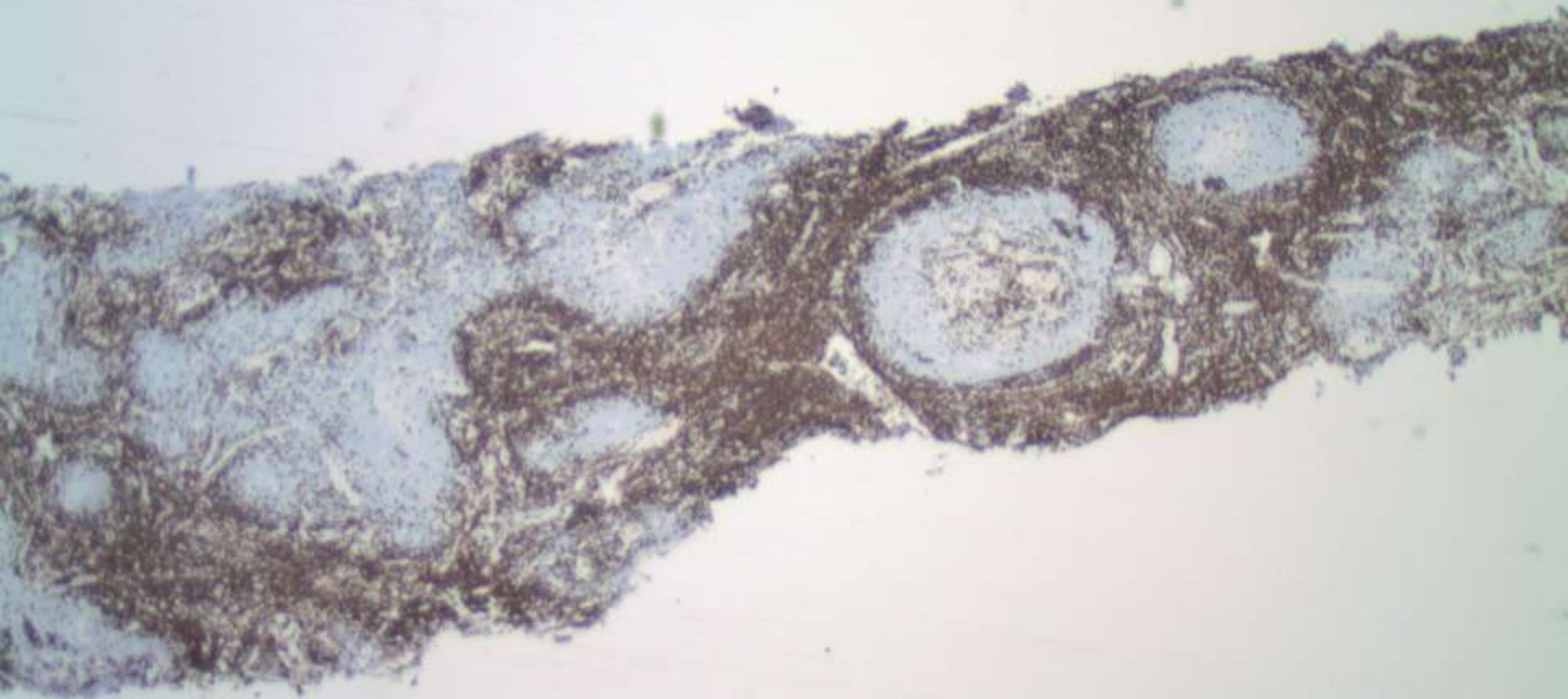
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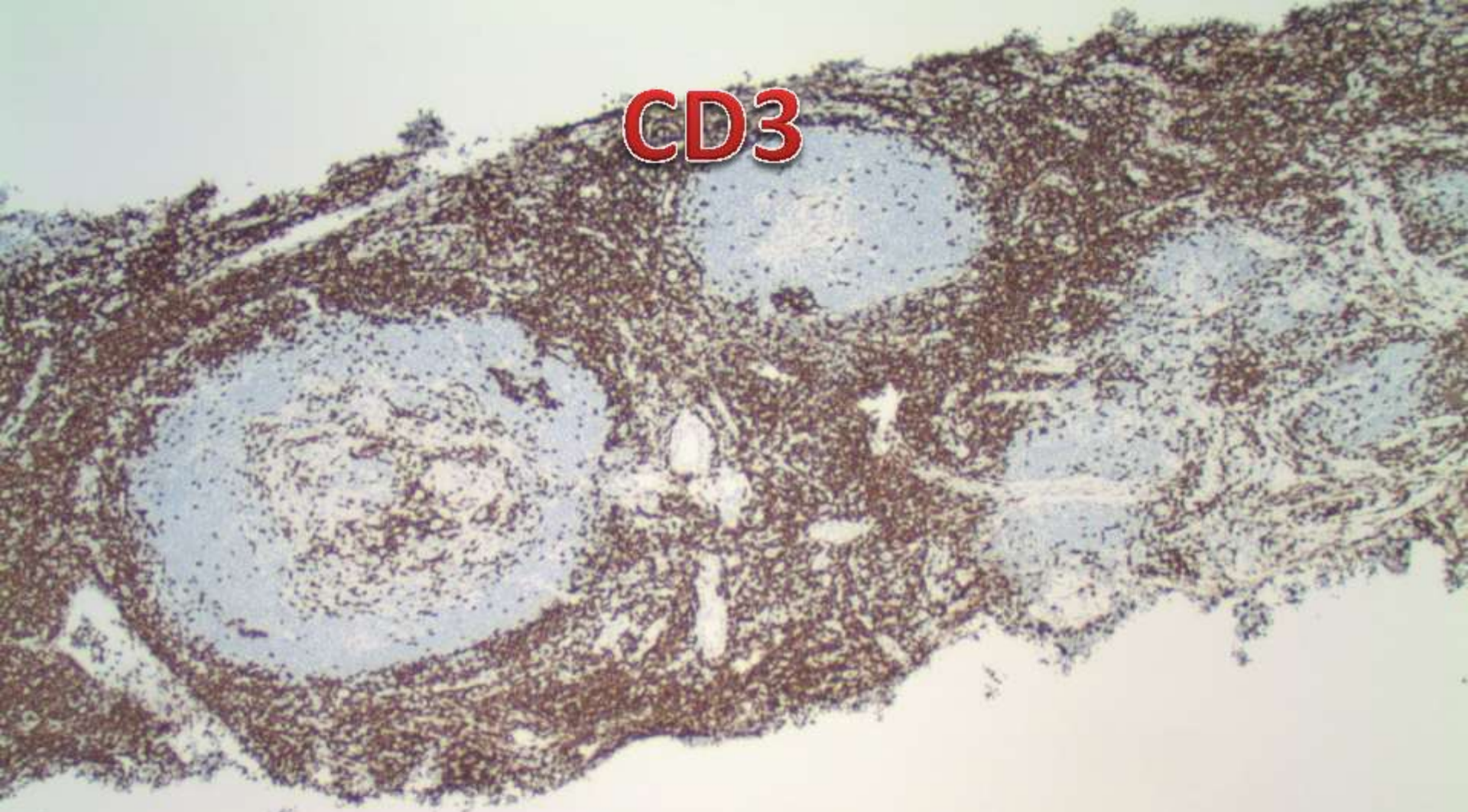
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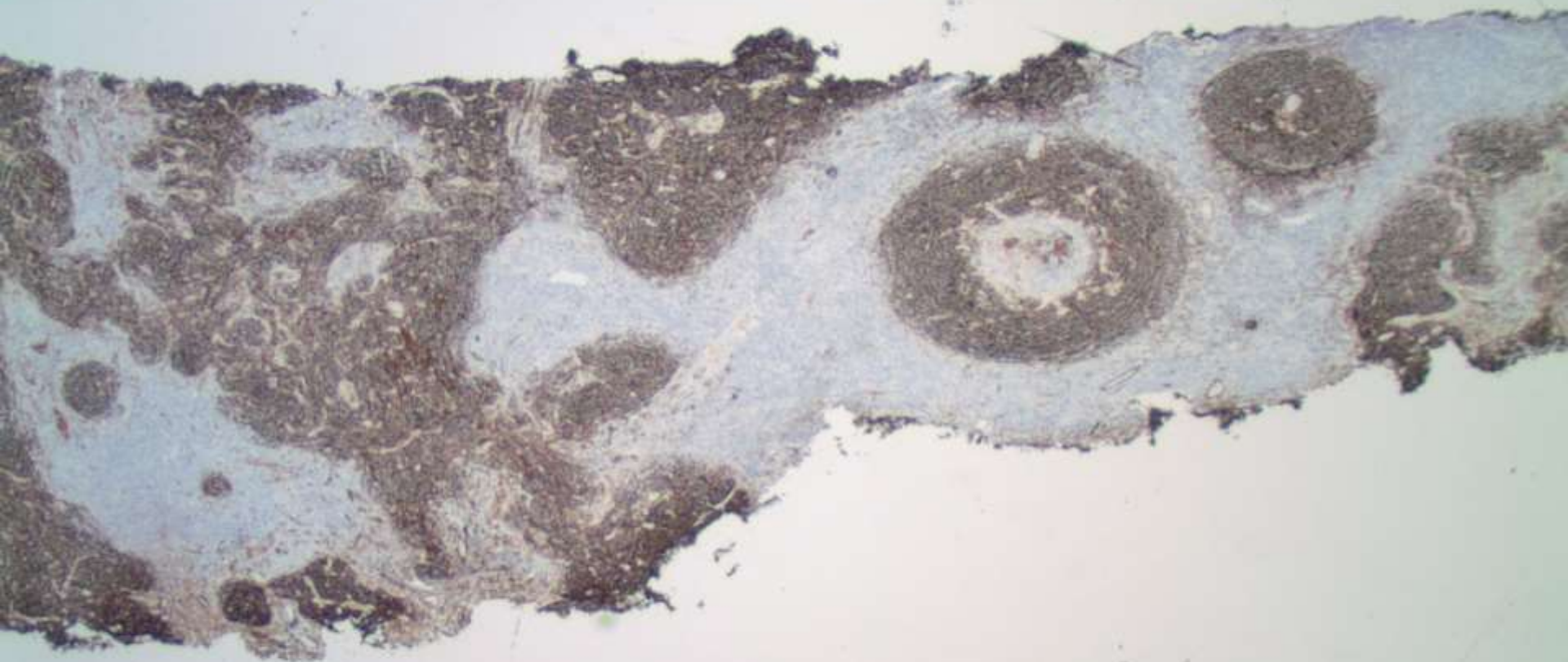
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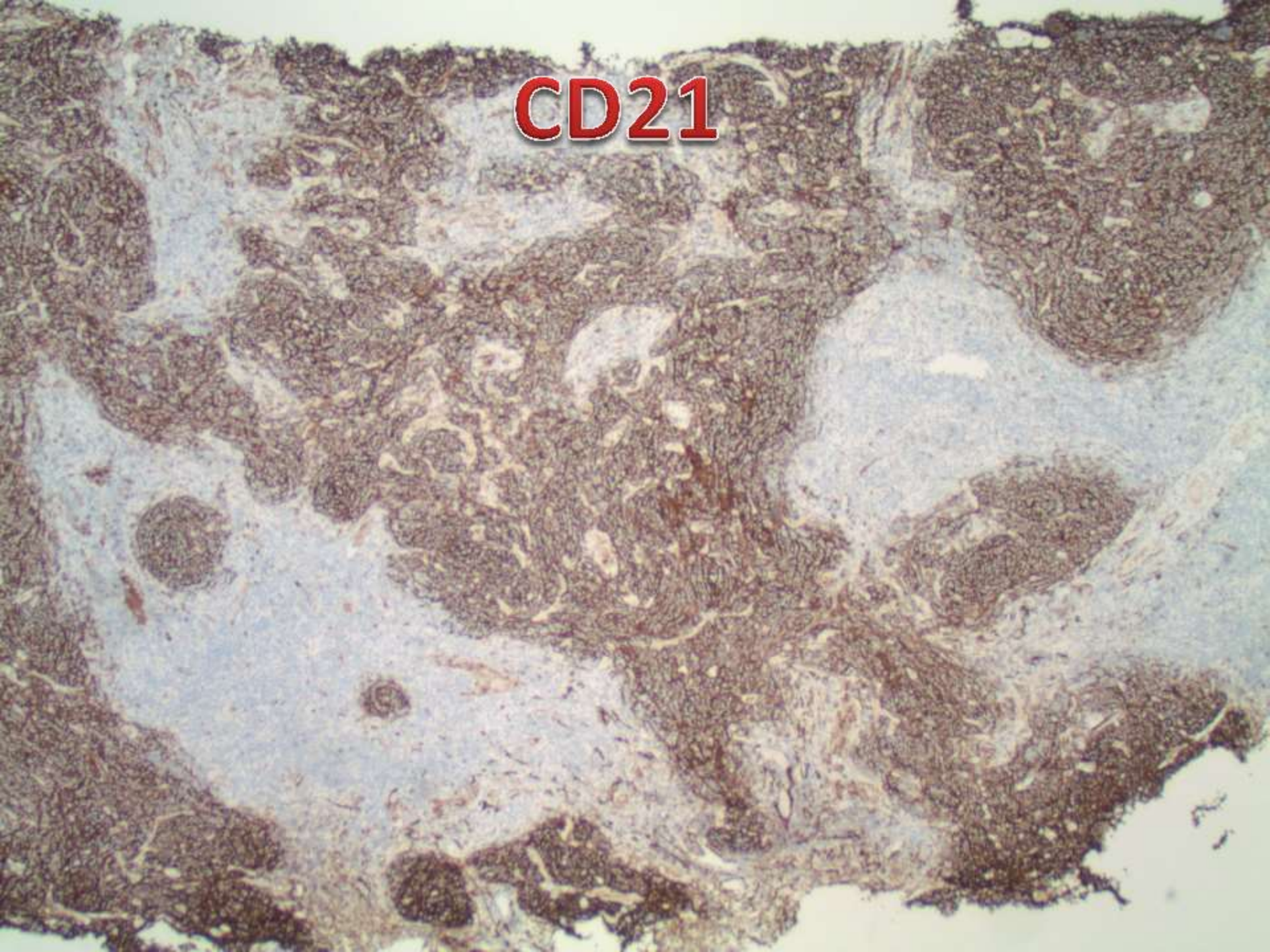
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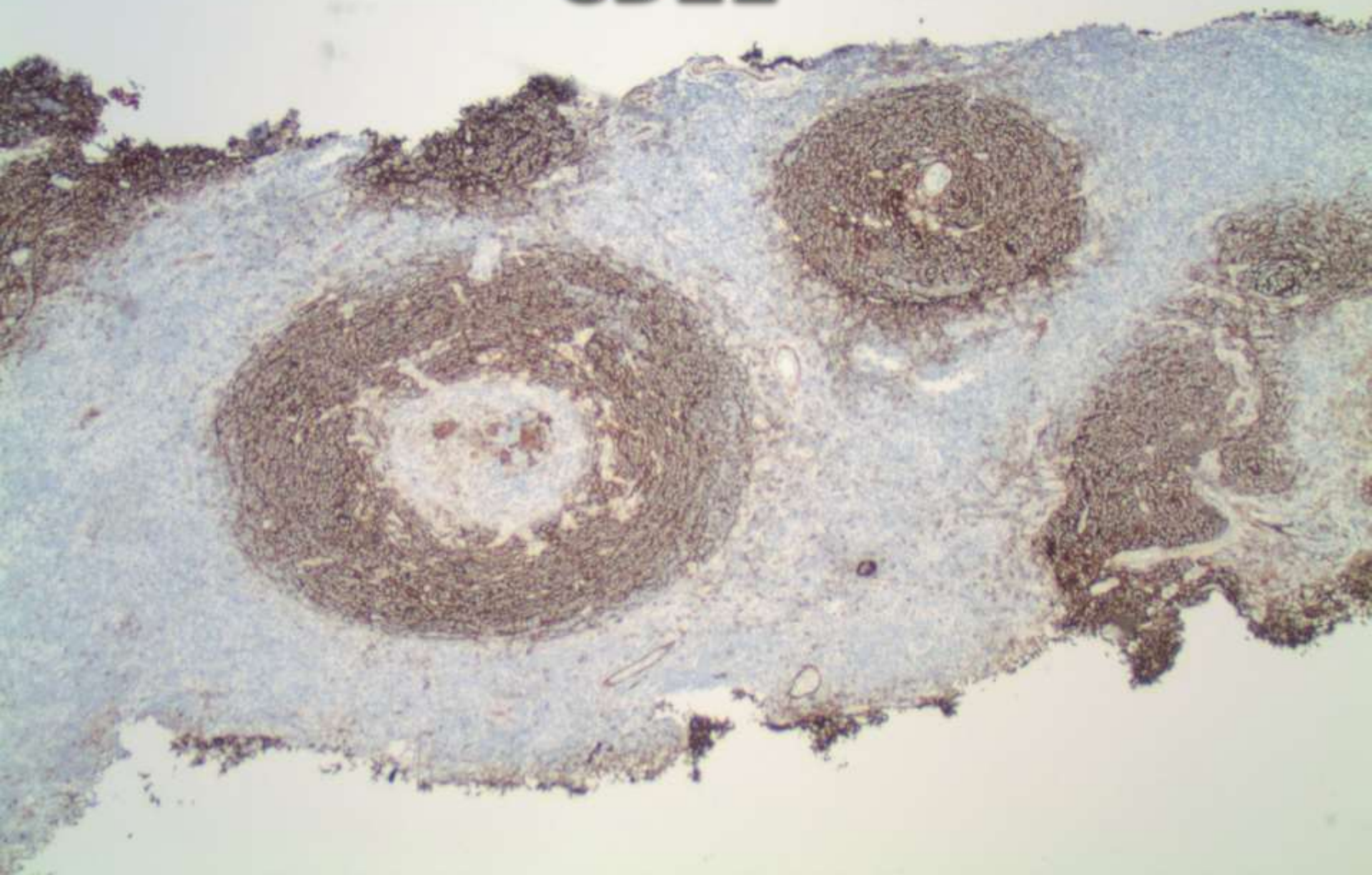
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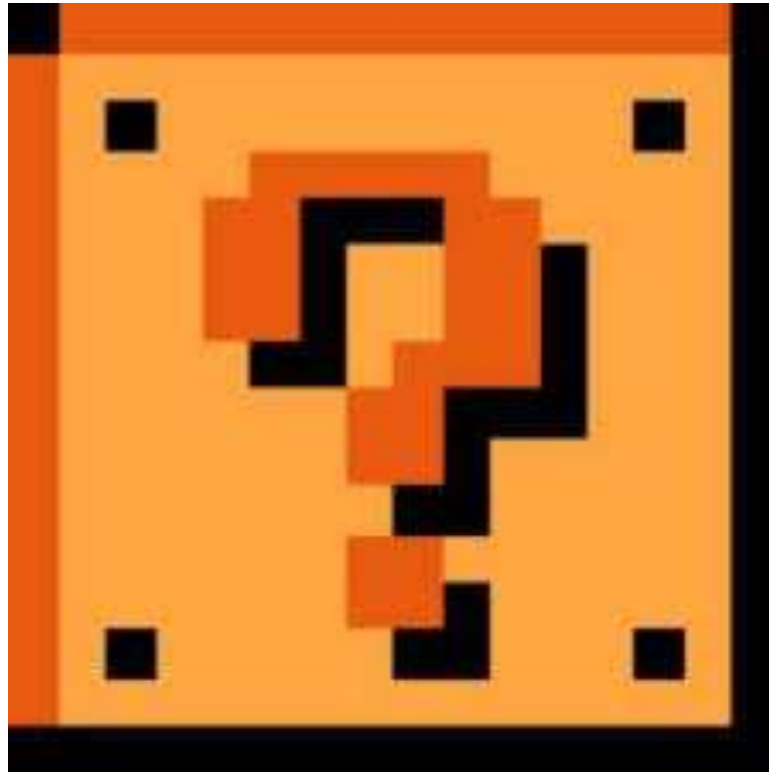
CD21



CD21

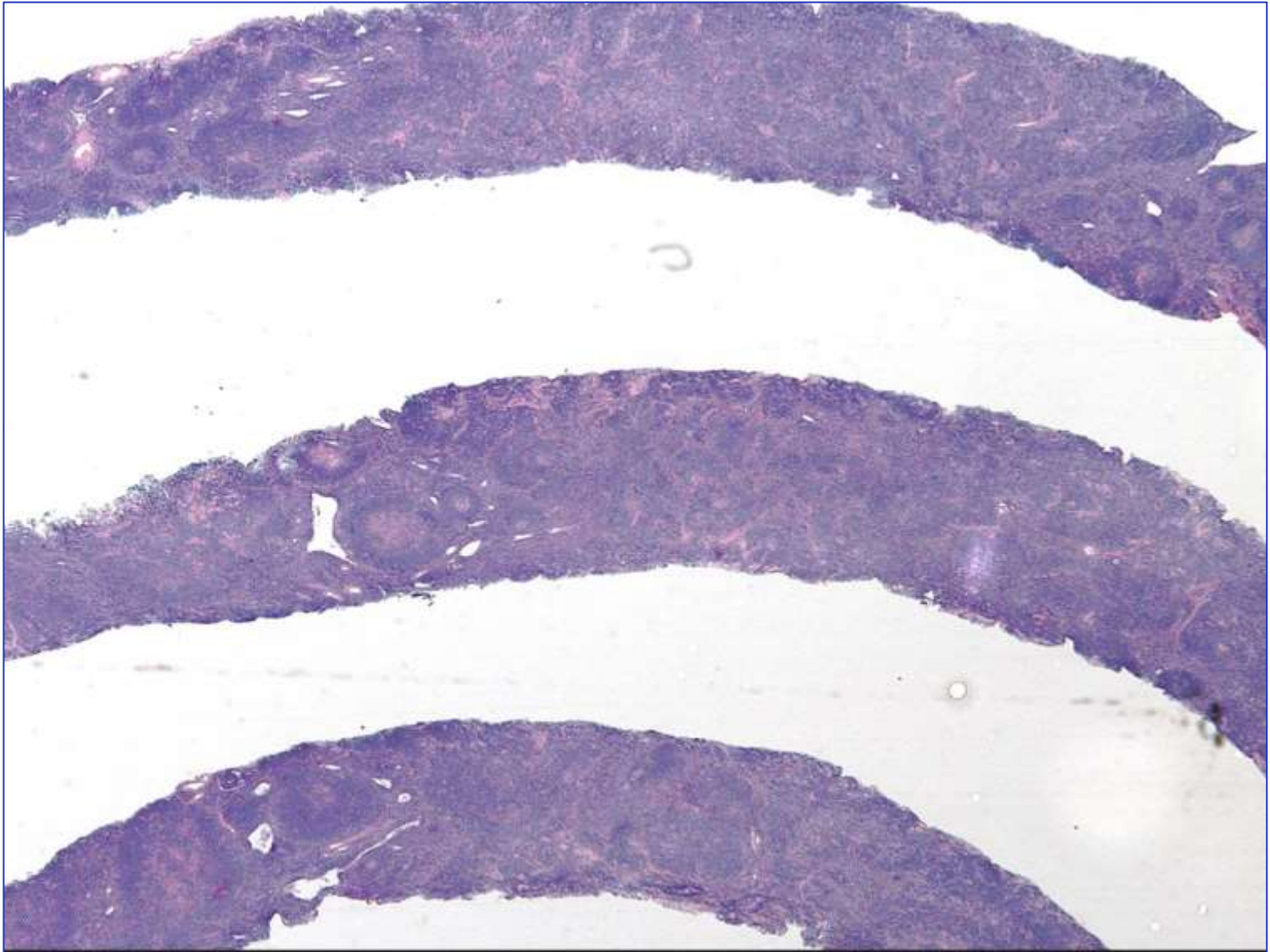


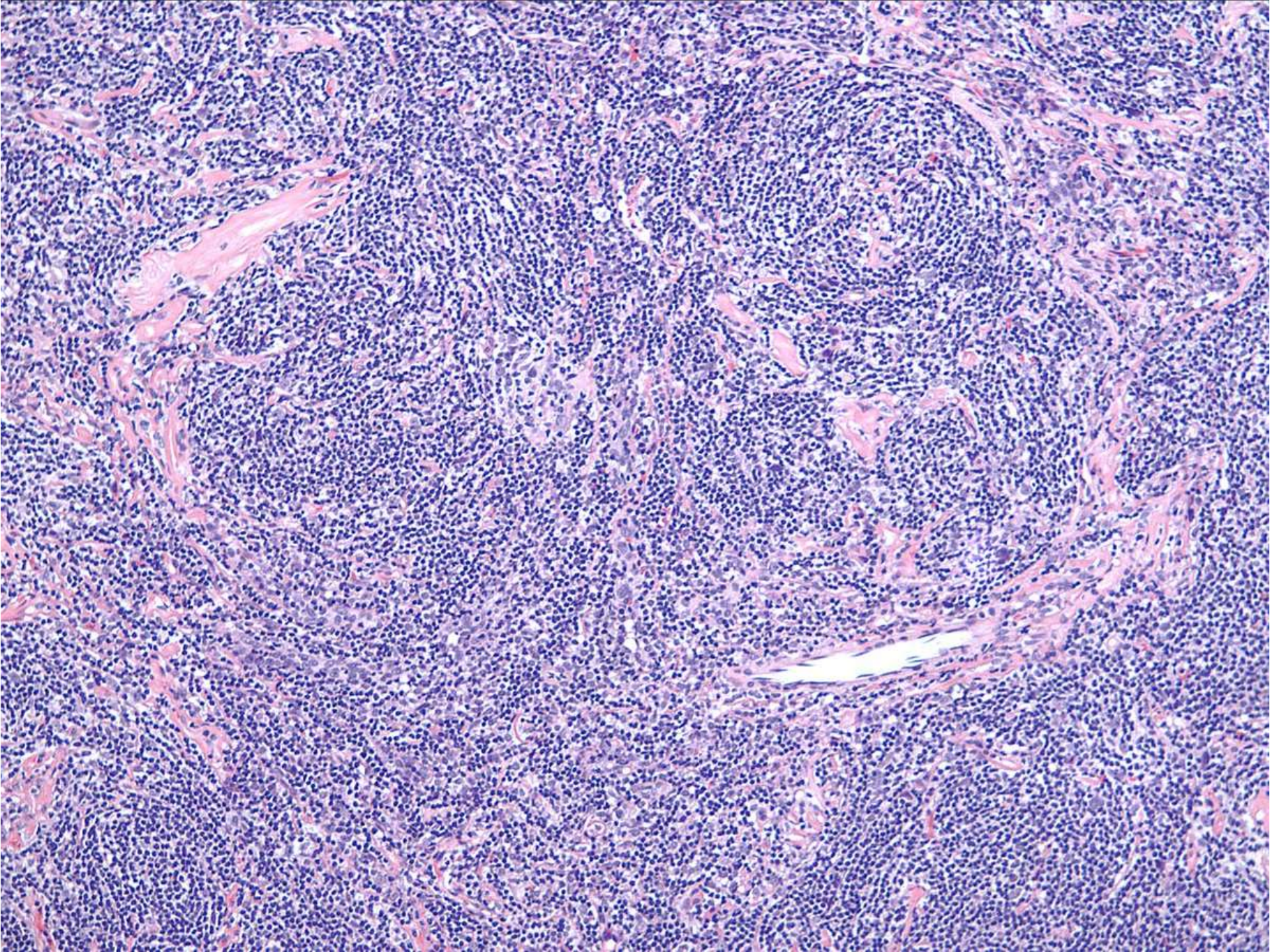
DIAGNOSIS?

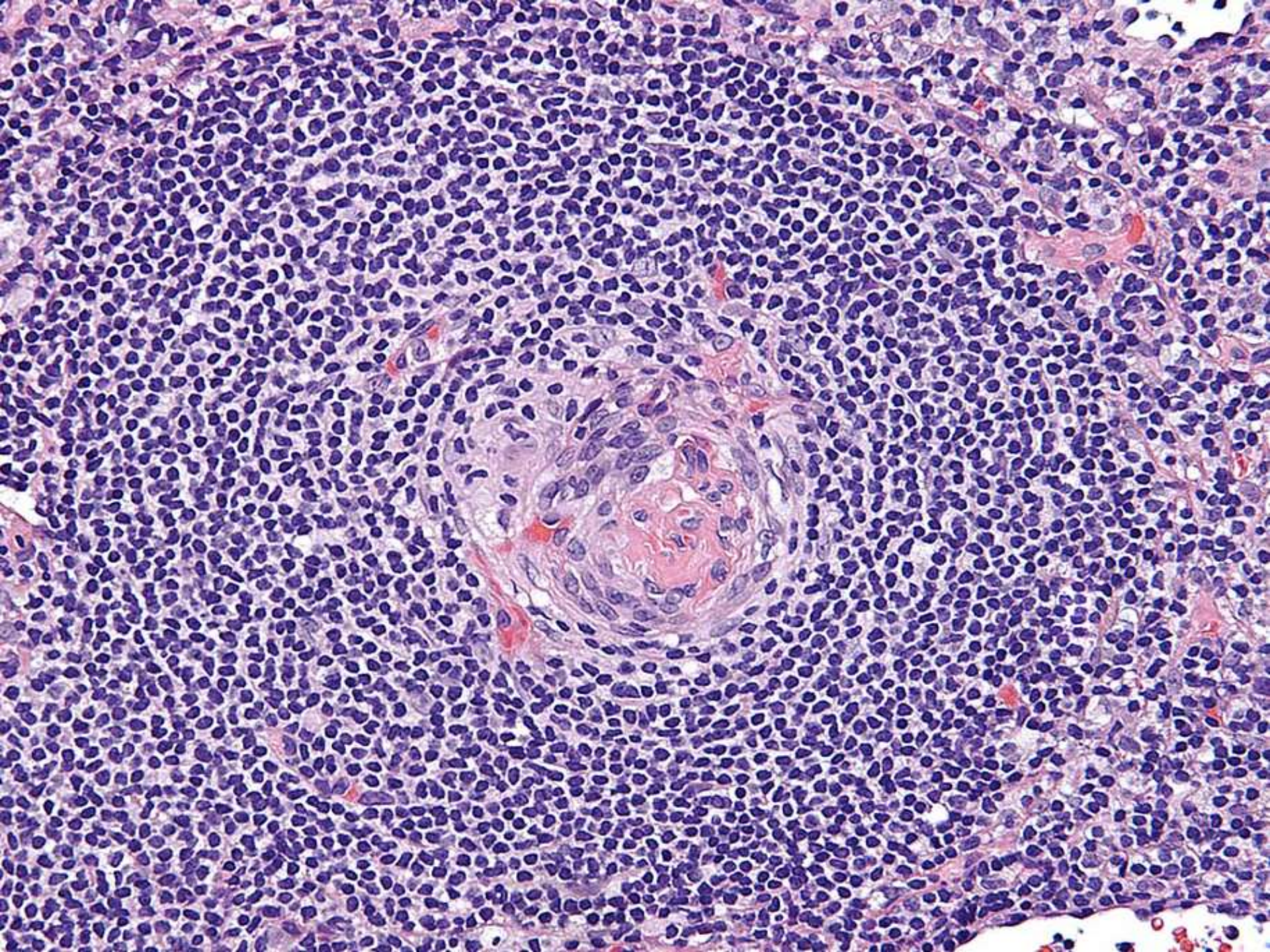


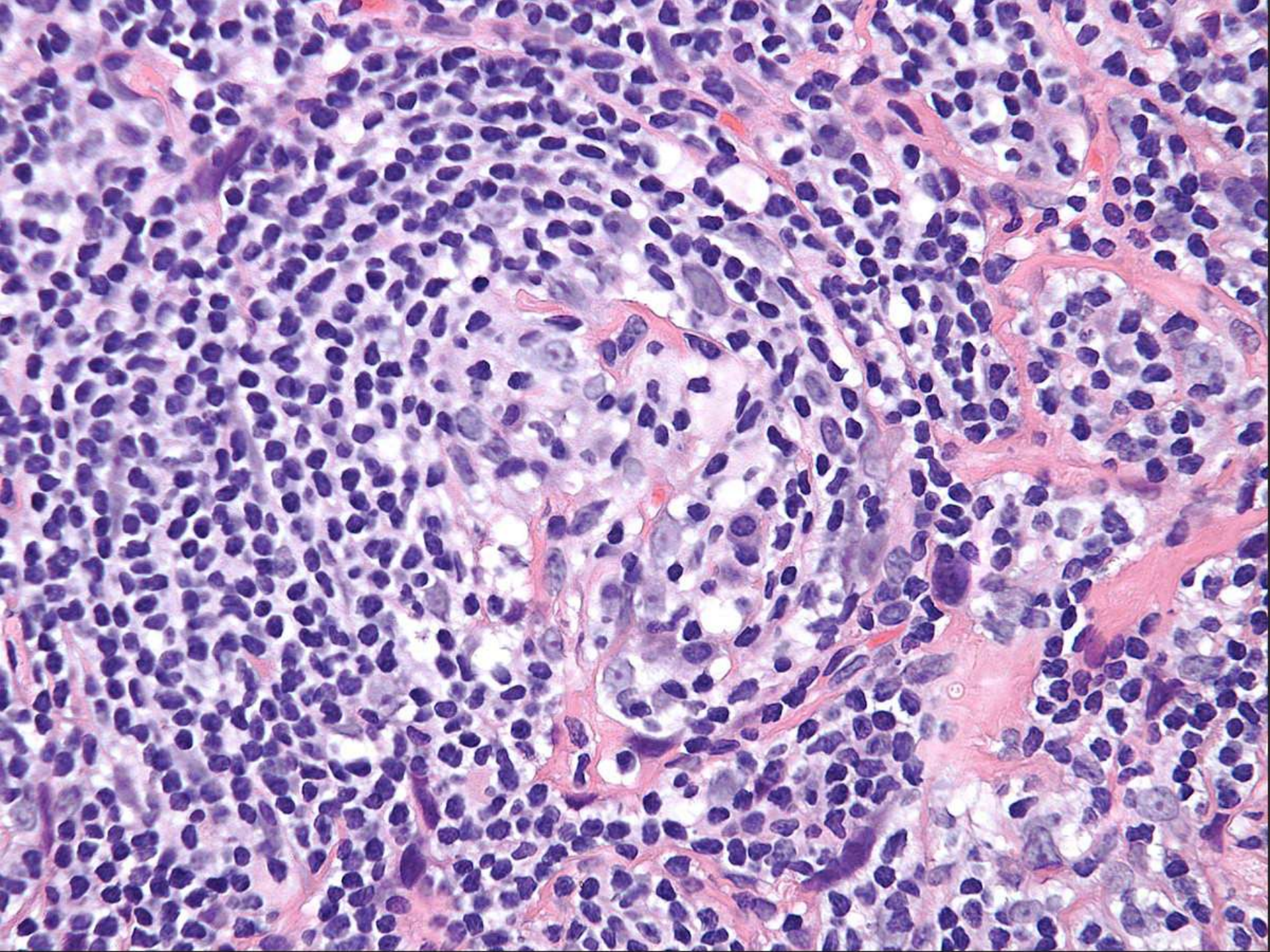
Clinical History

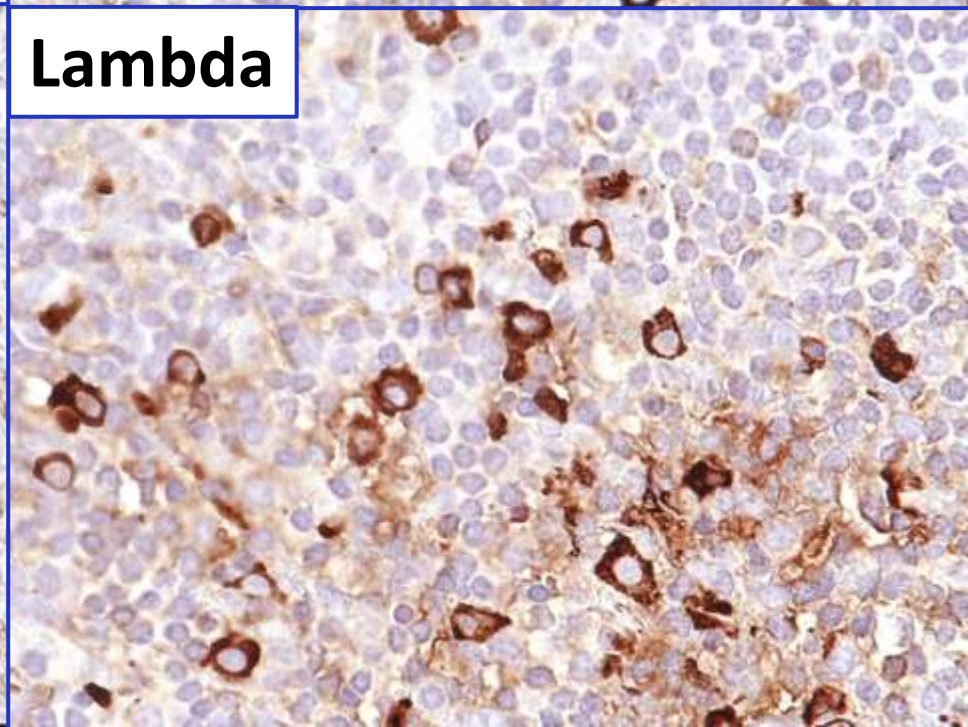
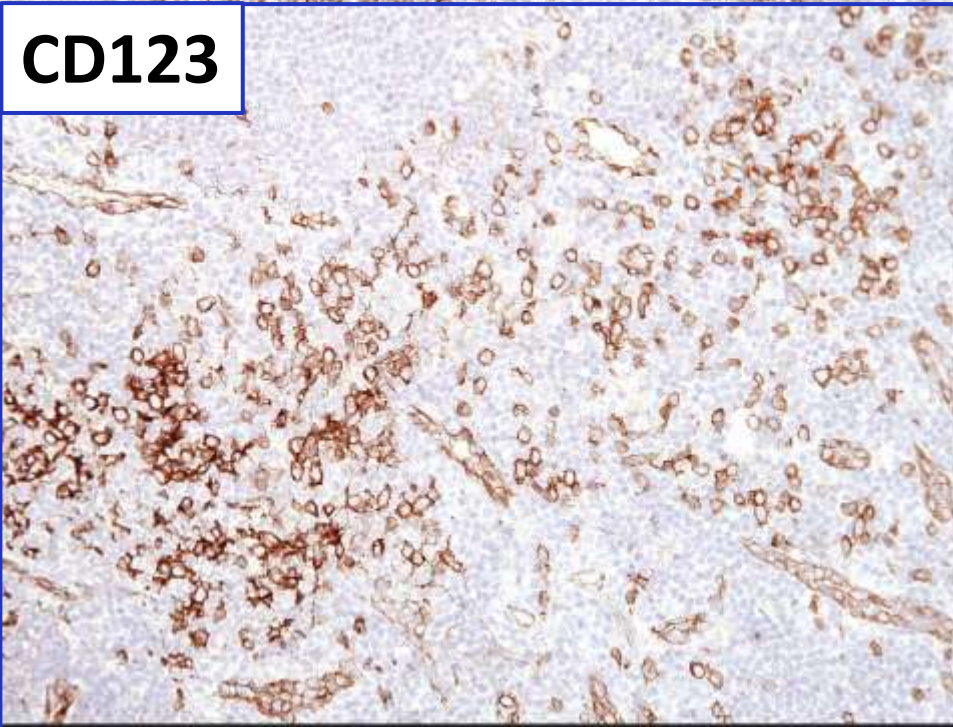
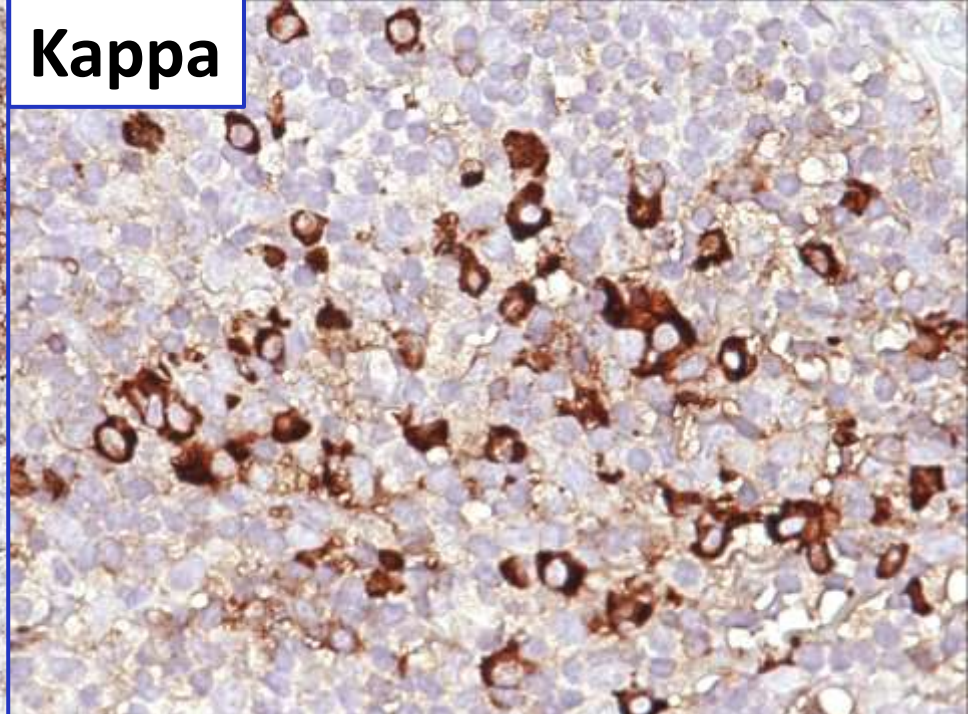
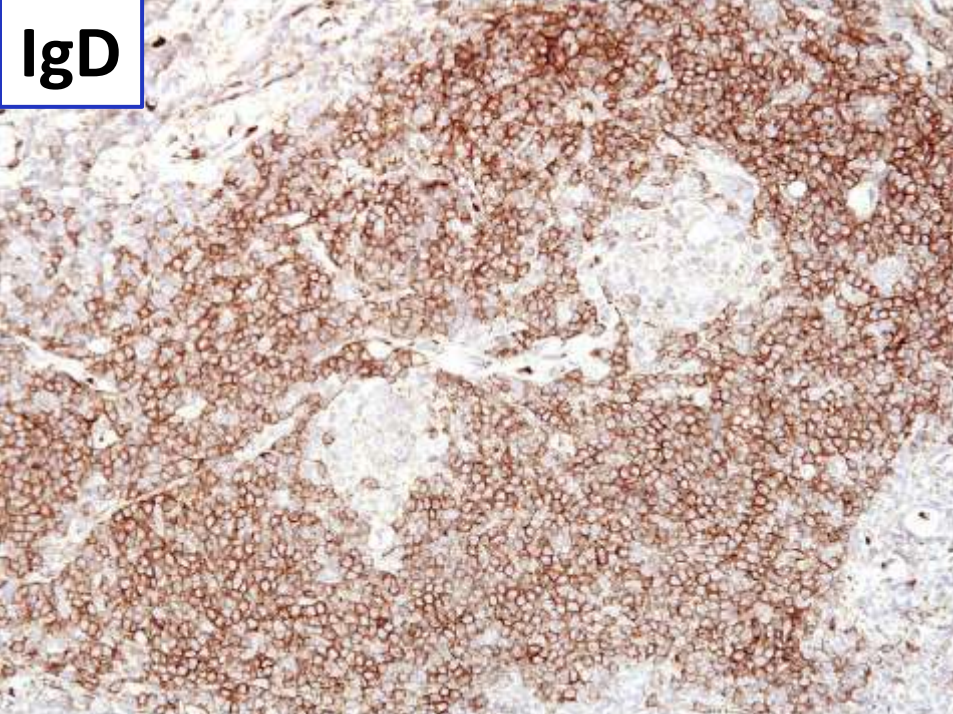
- 36-year old woman presenting with a palpable right axillary LN











Dx: Castleman Disease, Hyaline-Vascular Type

- Atrophic germinal centers
- Expanded mantle zones with “onion-skinning”
- Expansion/proliferation of follicular dendritic cells and plasmacytoid dendritic cells
- Increased plasma cells
- Prominent vessels
- Fibrosis

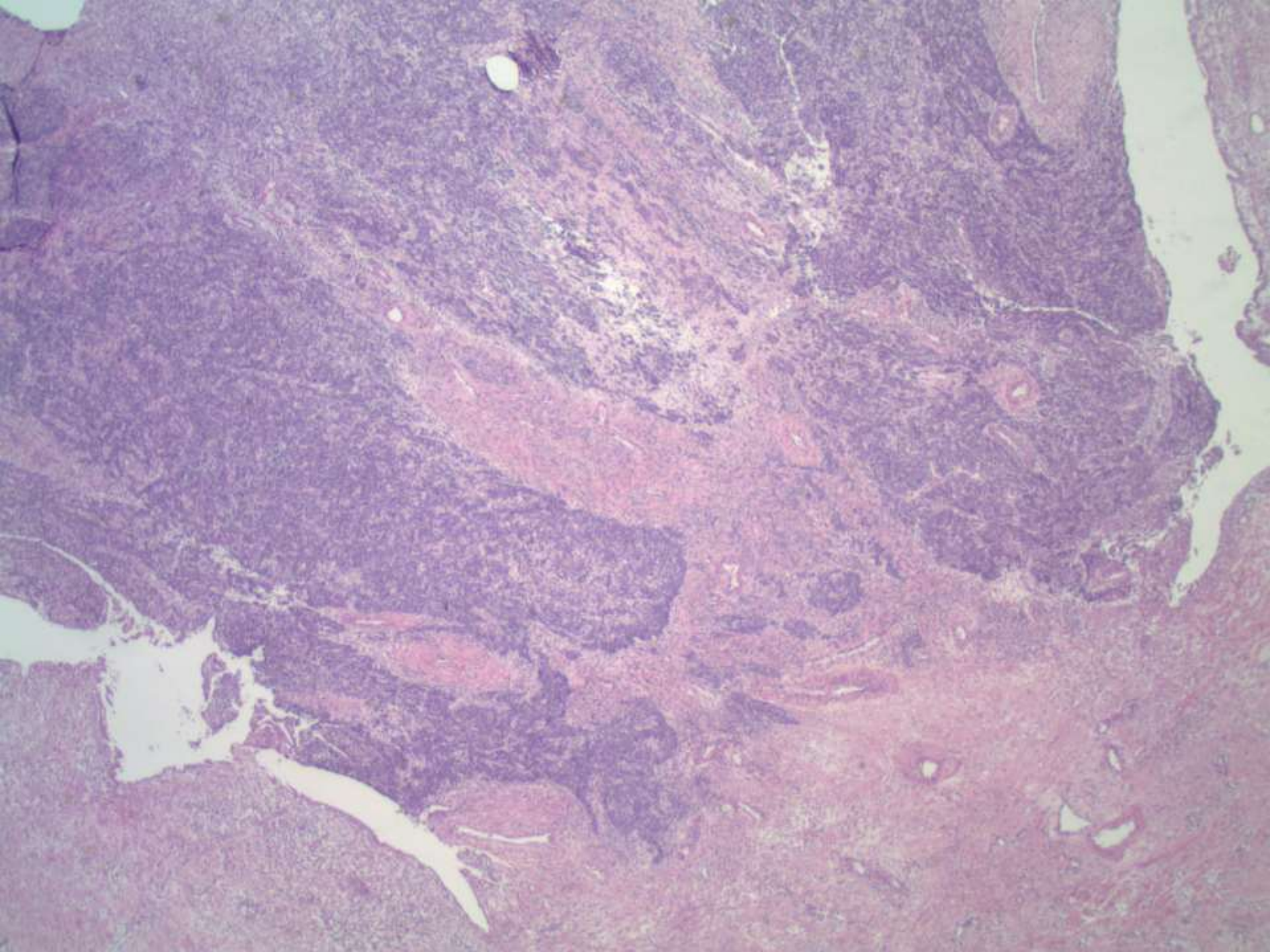
Castleman Disease

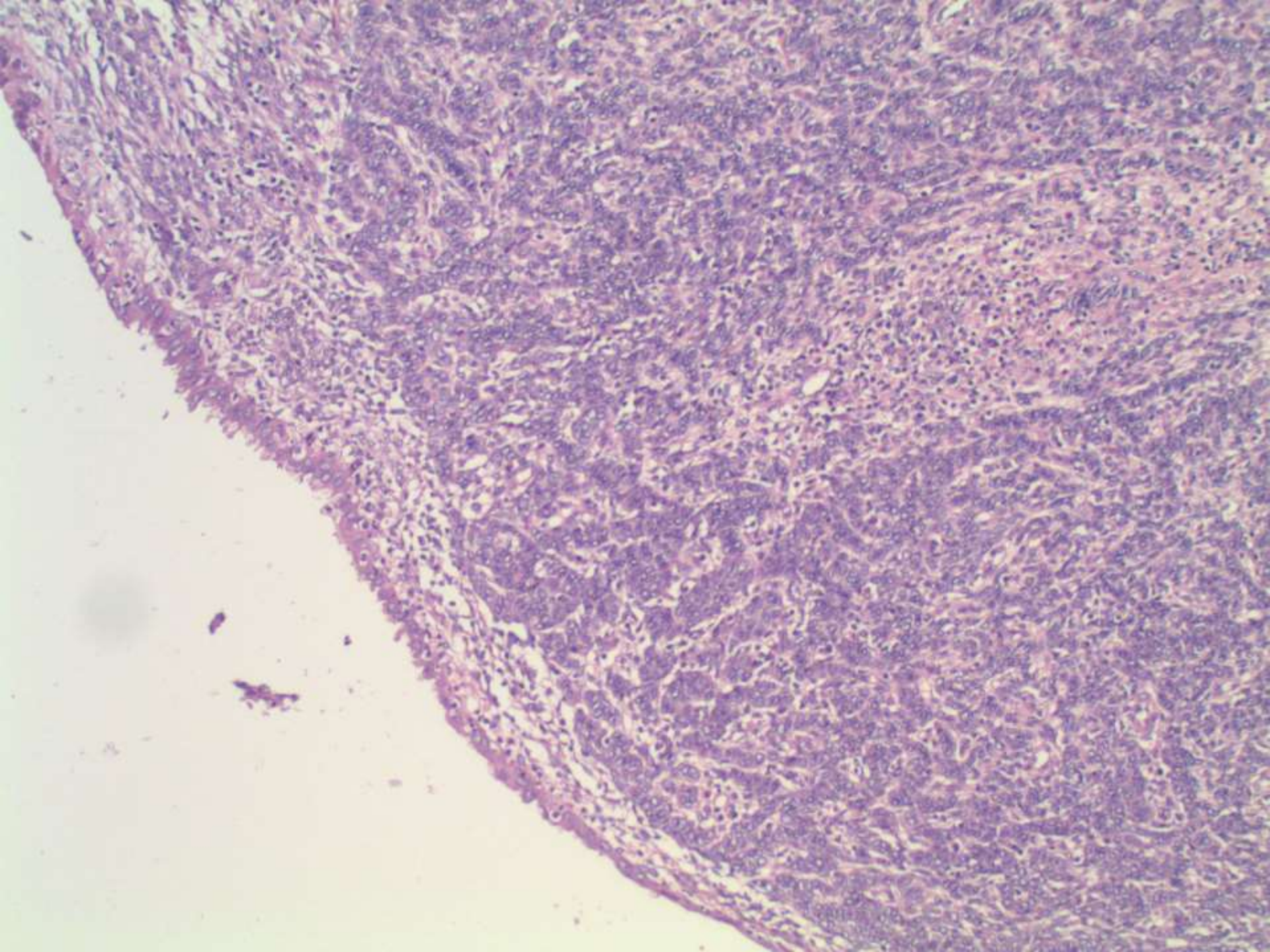
Type	Unicentric Hyaline-Vascular	Unicentric Plasma cell	Multicentric Castleman
Demographics	M = F, median 20 y	M = F, median 20 y	M = F, Median 50 y
Anatomic site	Single LN, often mediastinal; cervical, abdominal axillary	Single or aggregate of LN, most often abdominal	Multiple LN sites
Symptoms	Rarely symptomatic	Systemic symptoms	Systemic symptoms, hepatosplenomegaly, POEMS in 15%
Pathogenesis	Unknown	Increased IL-6	Increased IL-6 HHV8 & HIV+/-
Management	Excision almost always curative	Excision almost always curative	Anti-IL6, chemo tx, radio tx, steroids

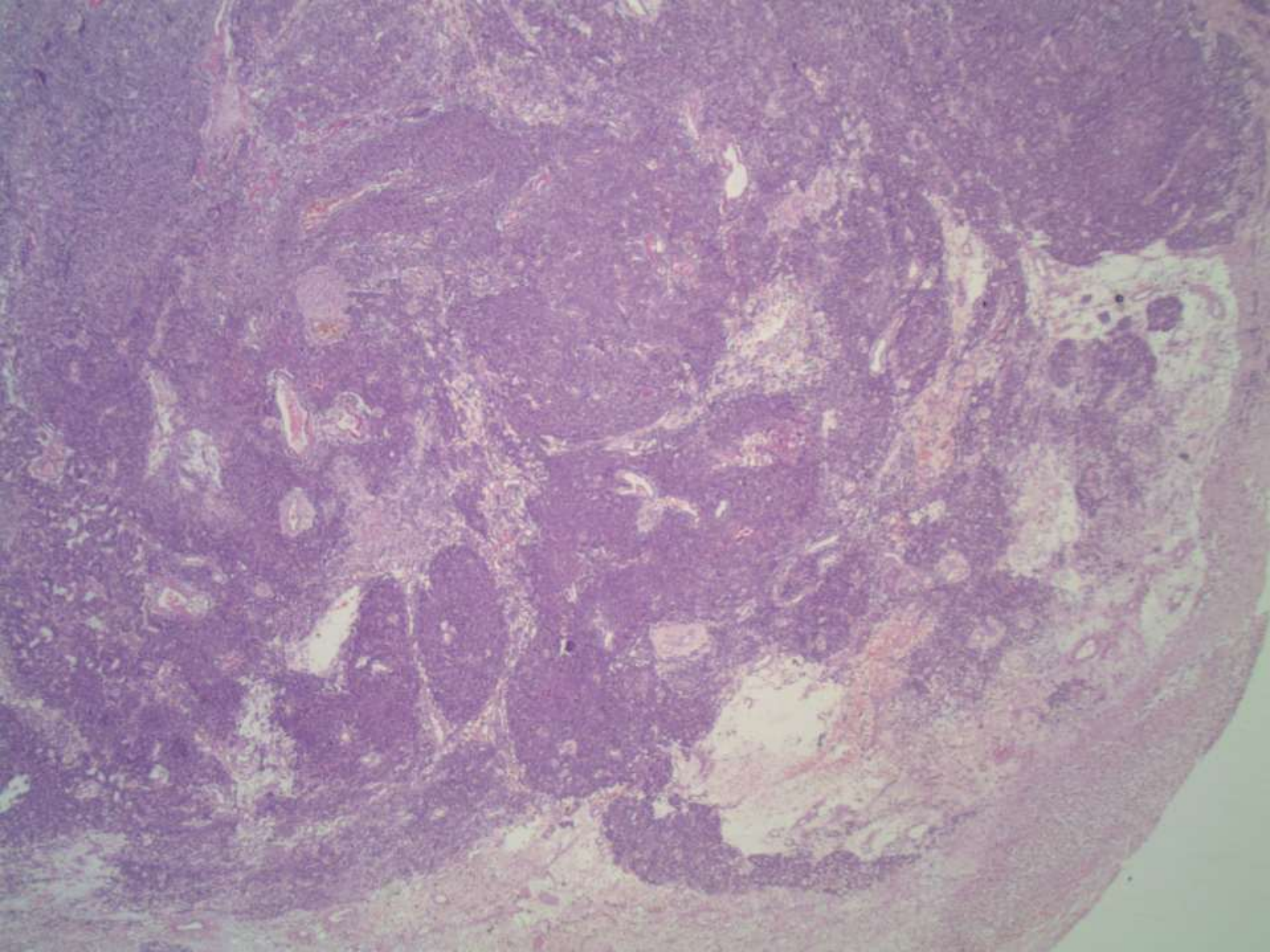
SB 6046

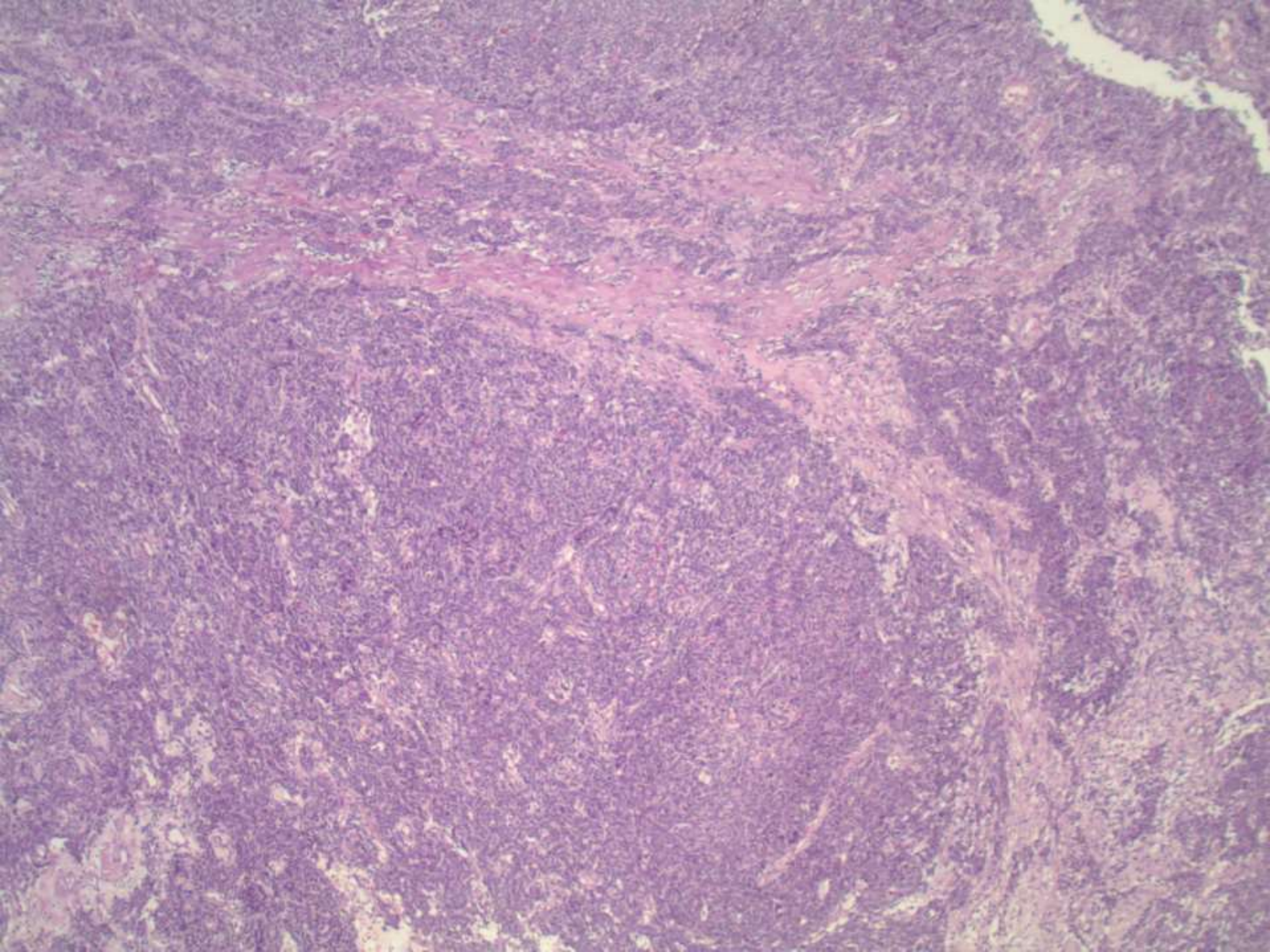
Nabeen Nayak; Sir Ganga Ram Hospital, New Dehli

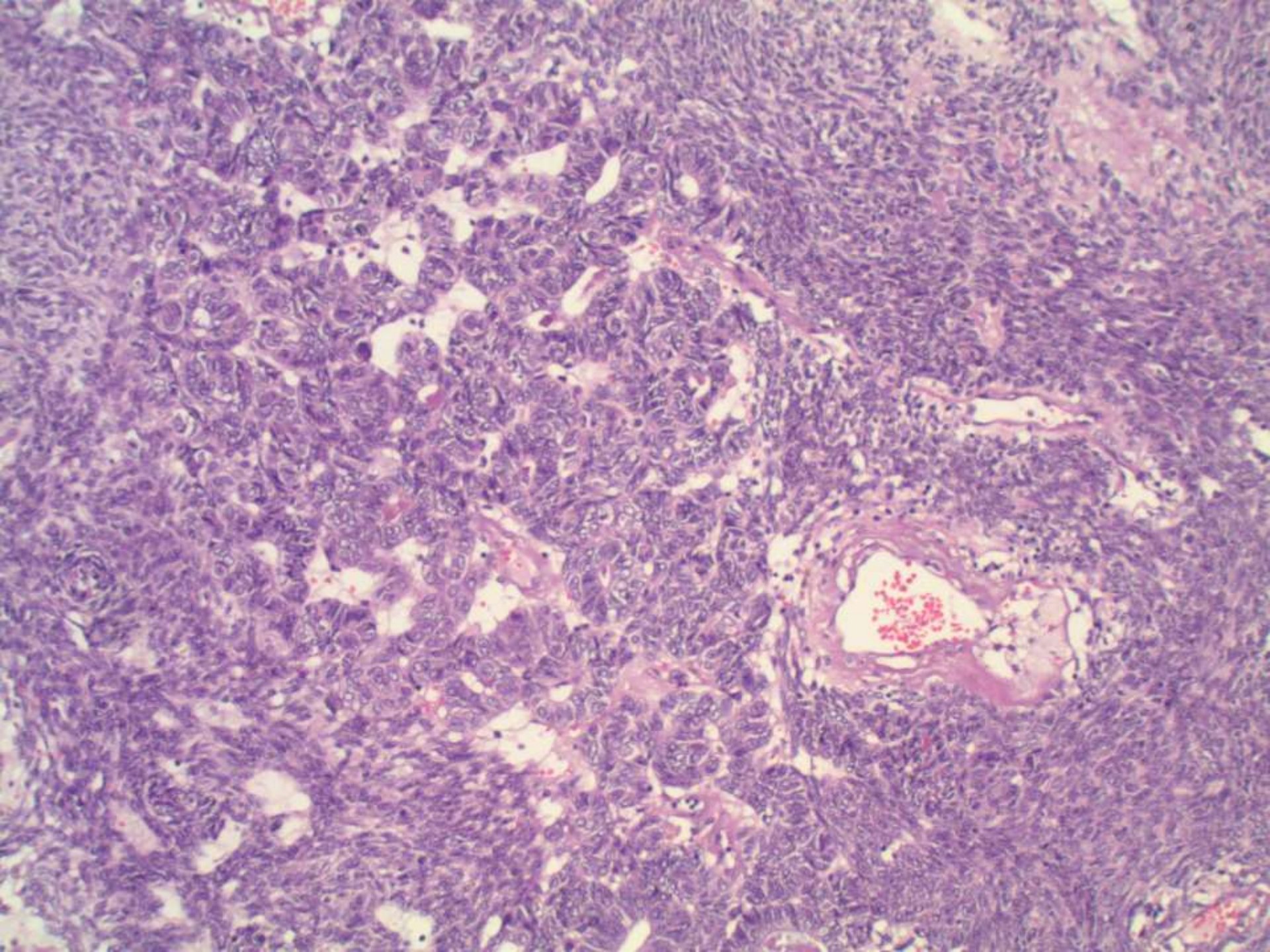
42-year-old female had bilateral tubo-ovarian masses clinically assessed as infective, uterus and cervix were unremarkable. Endoscopic left salpingo-oophorectomy and right salpingectomy done. Left intra-tubal mass seen.

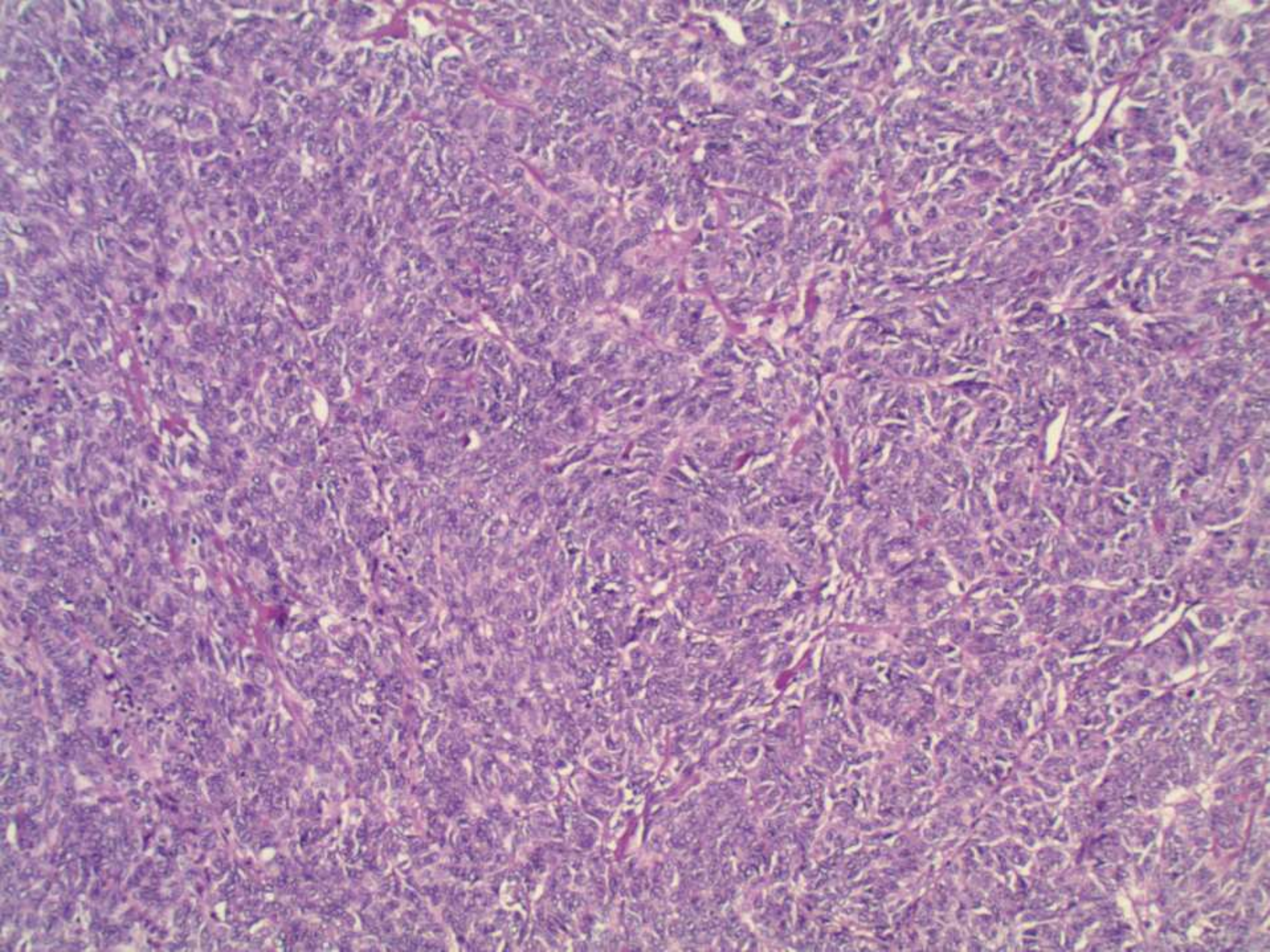


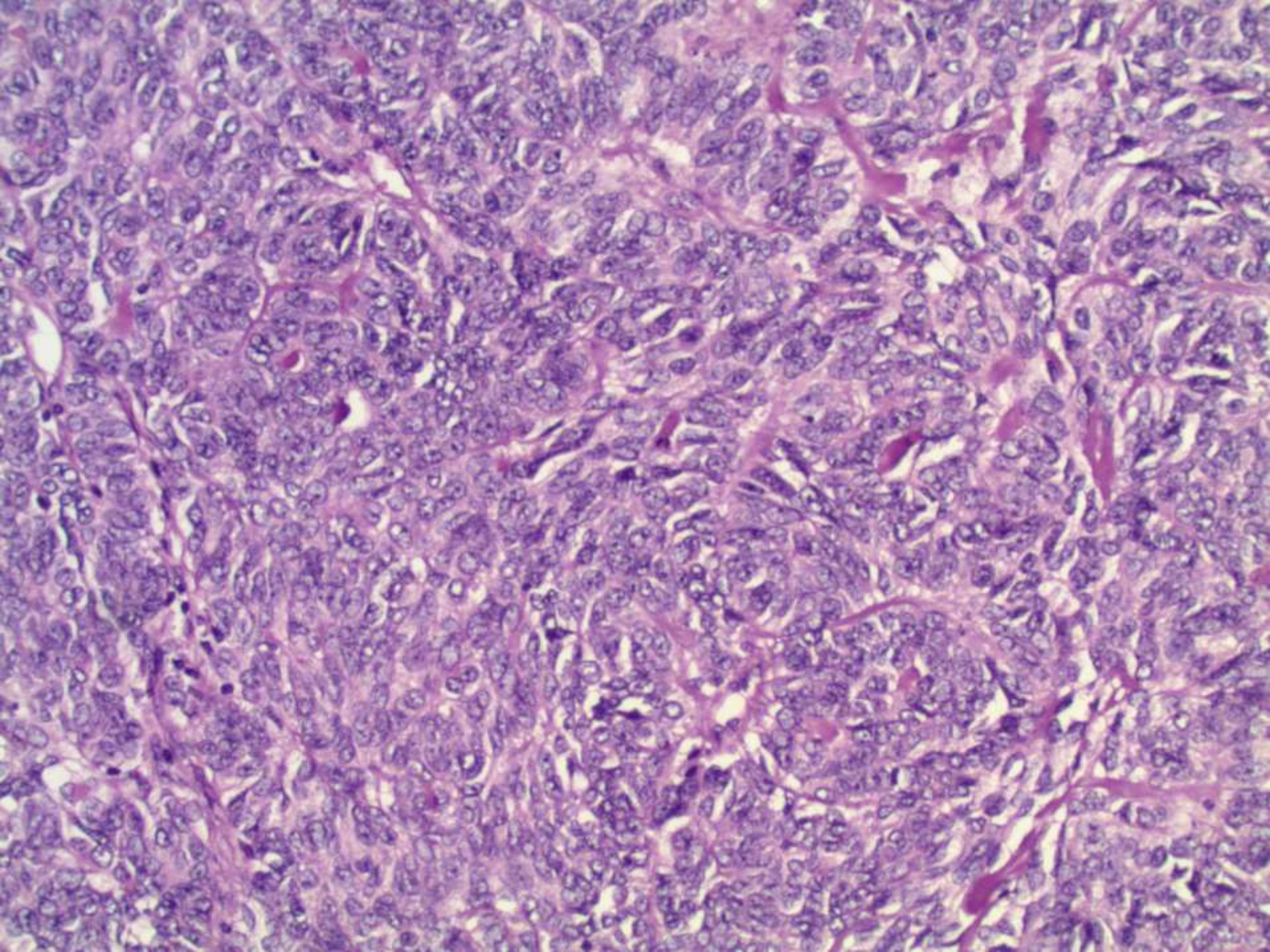


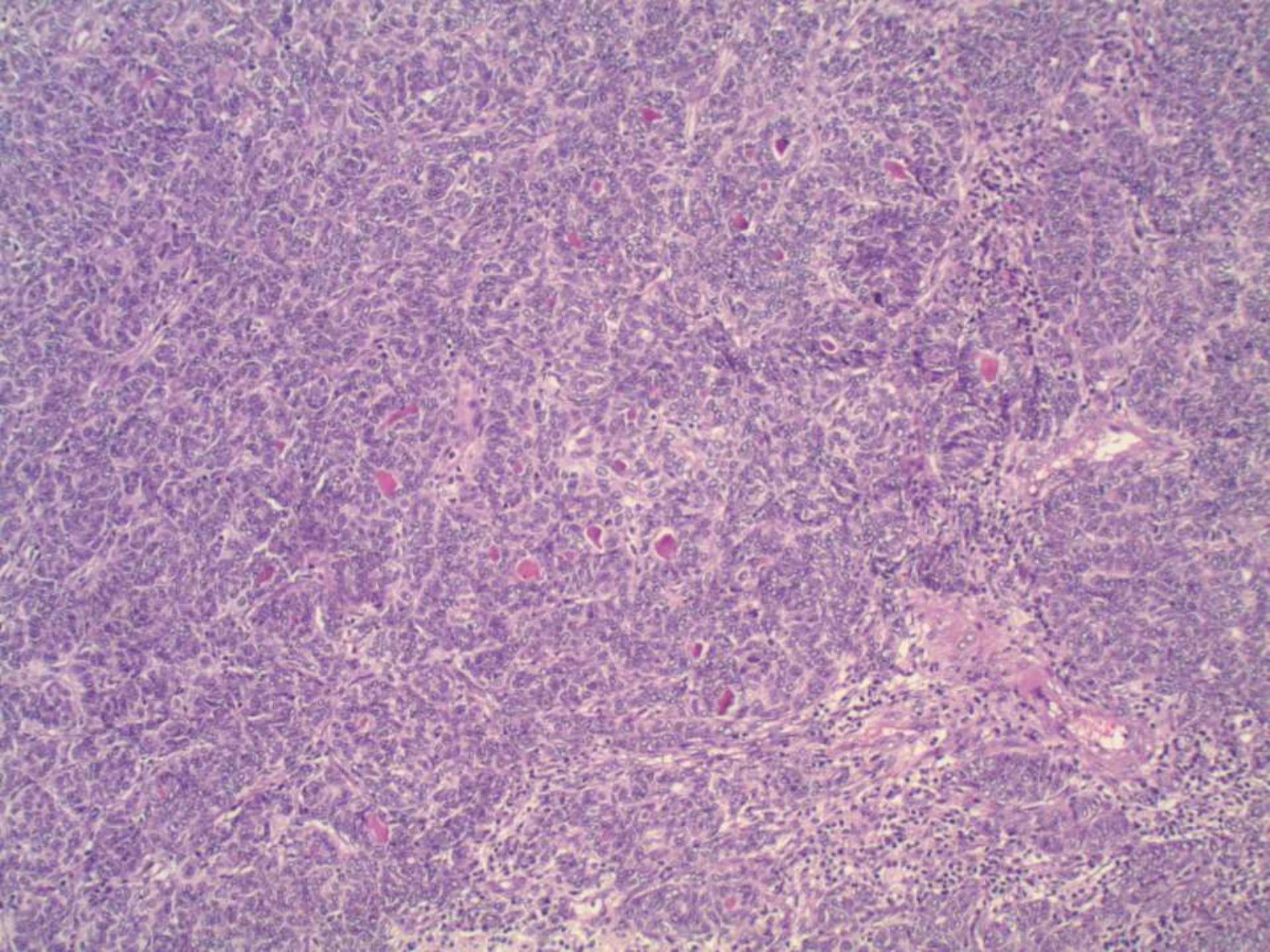


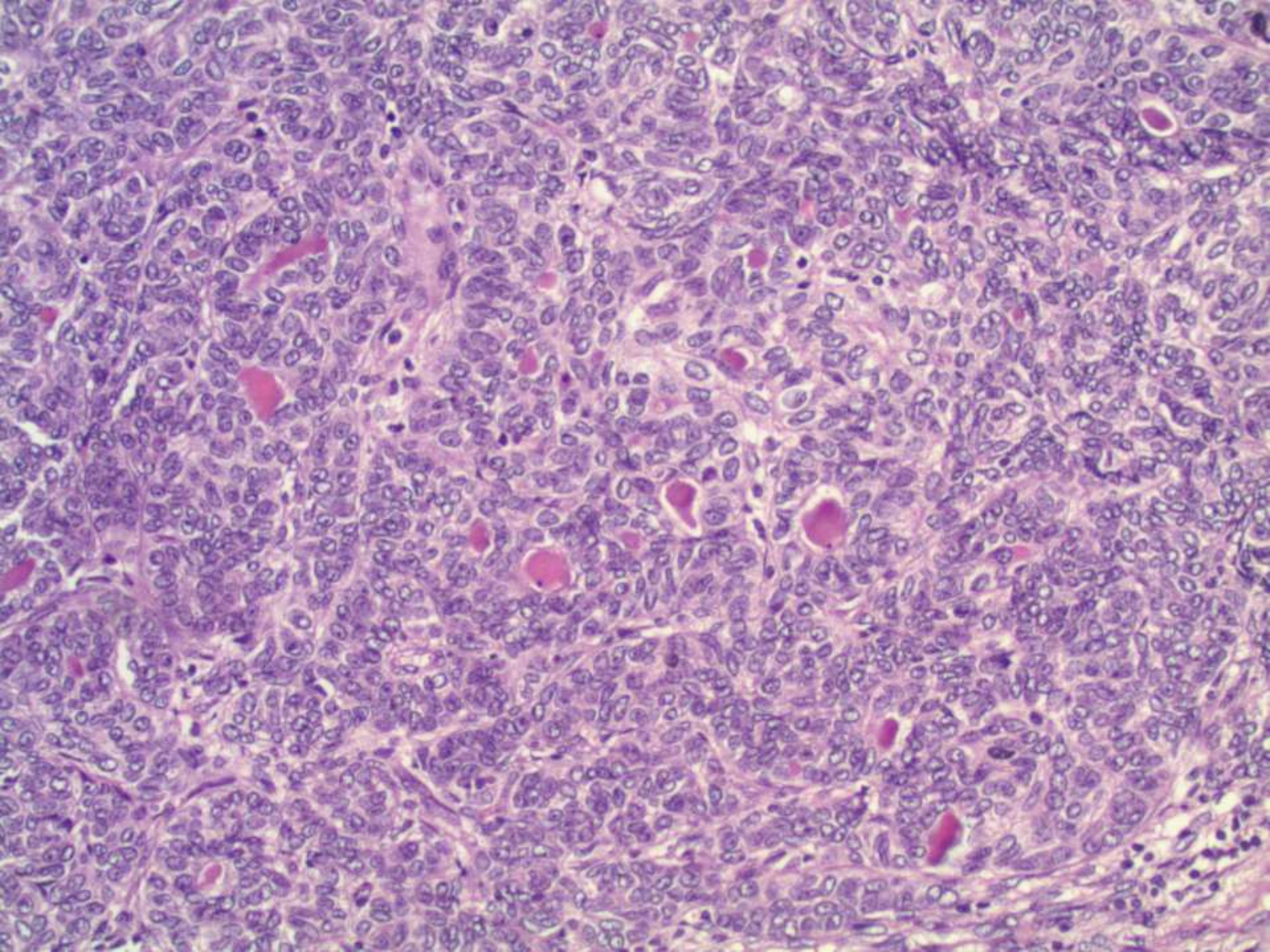


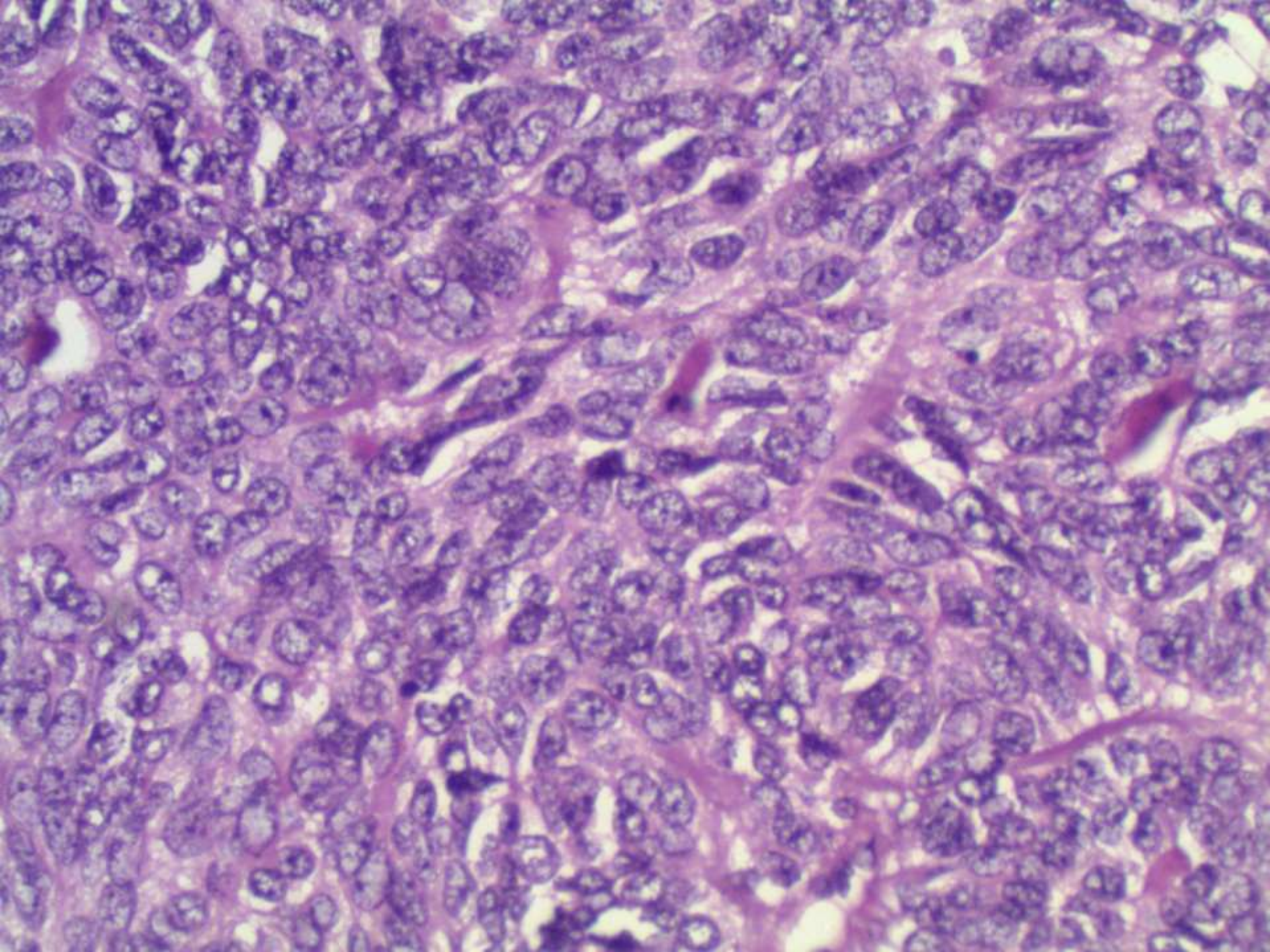




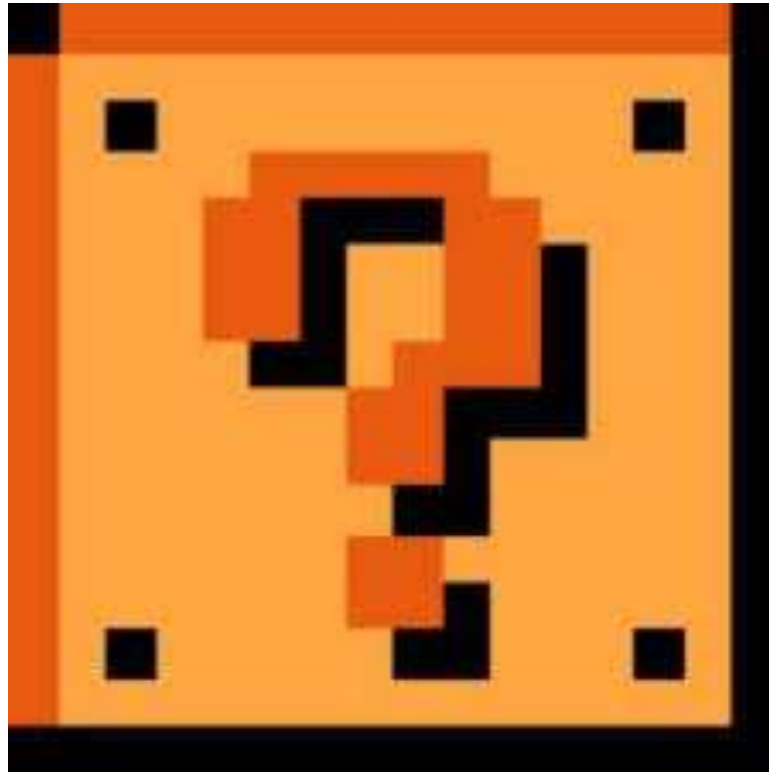


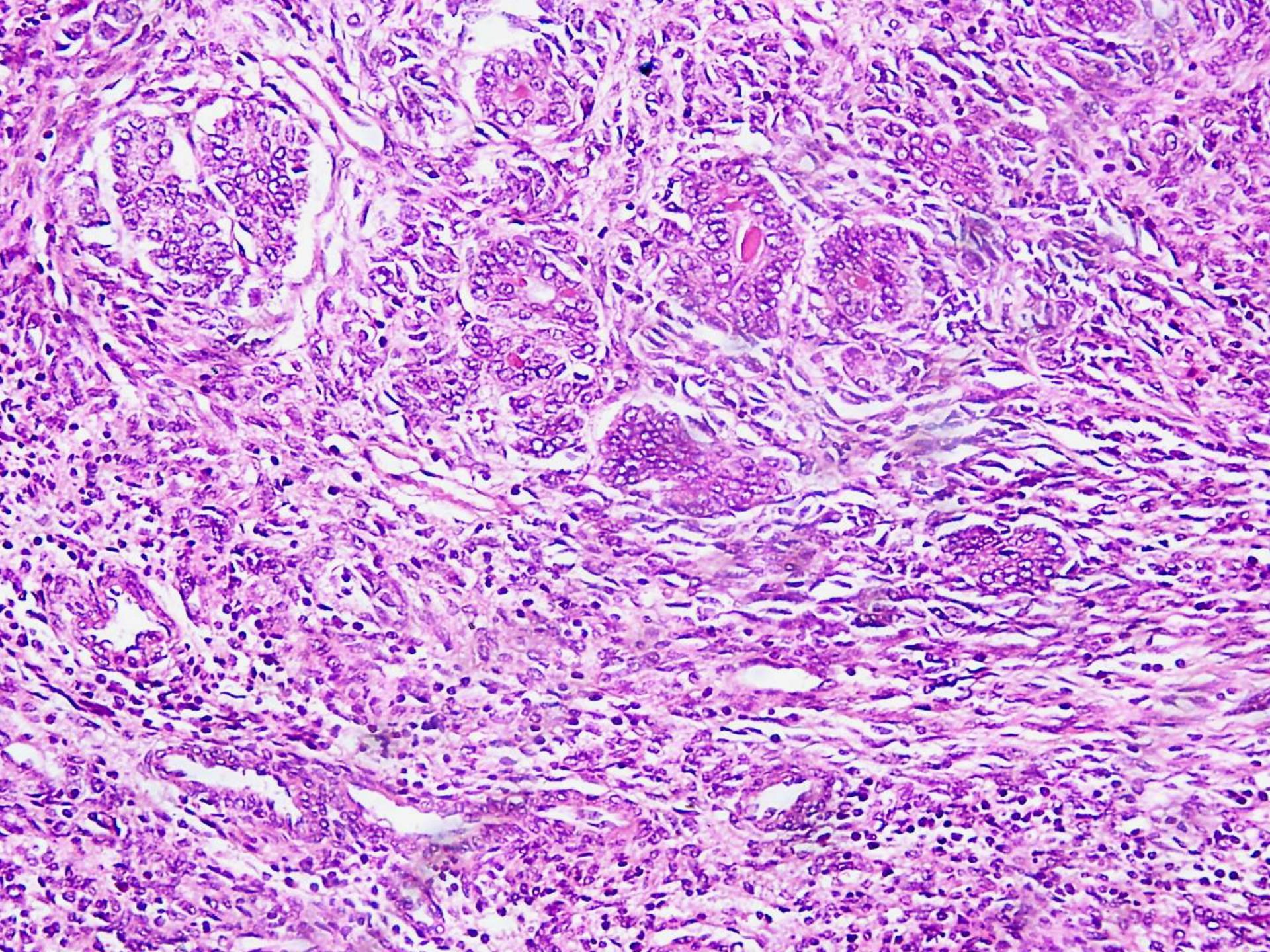


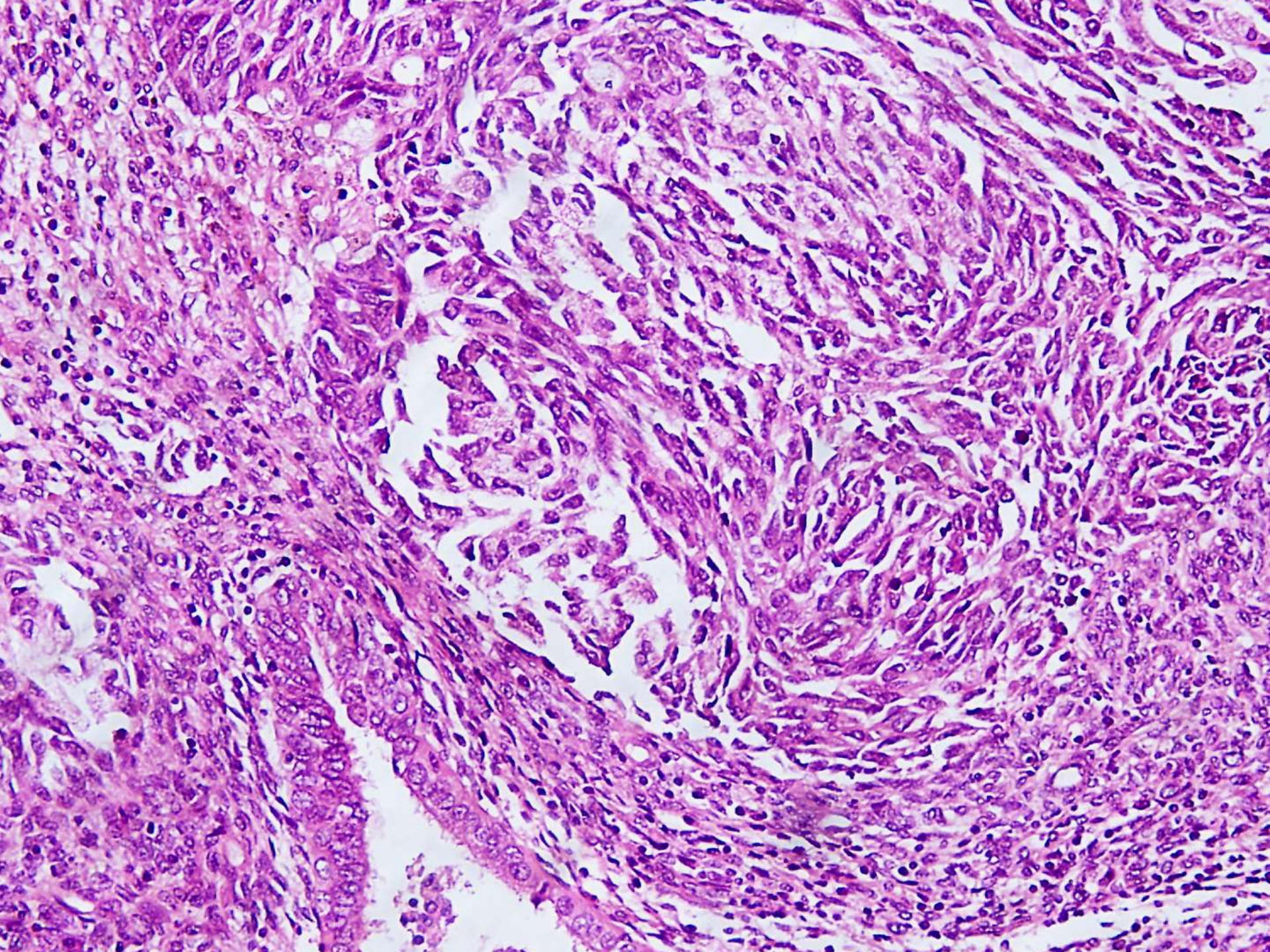


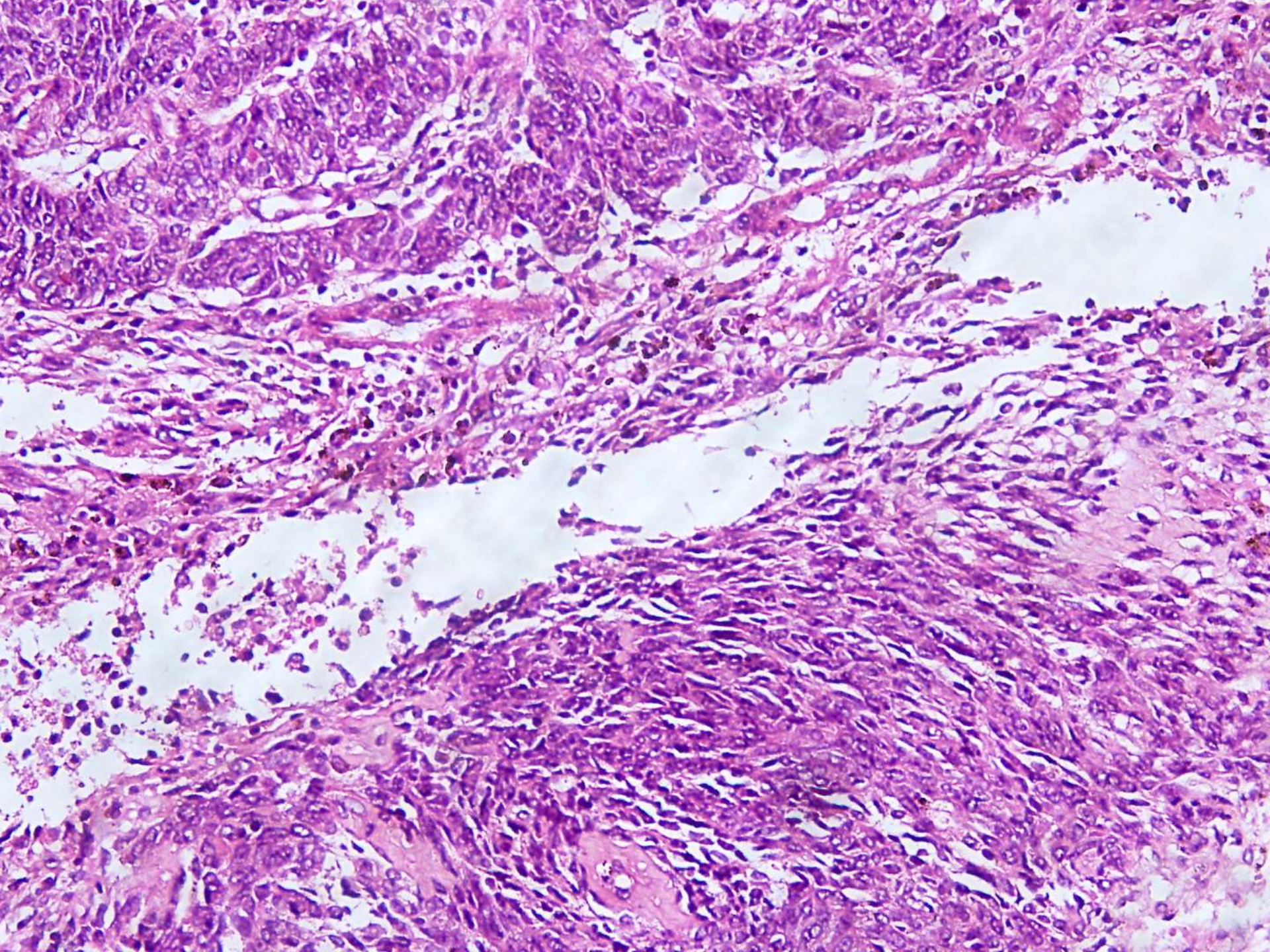


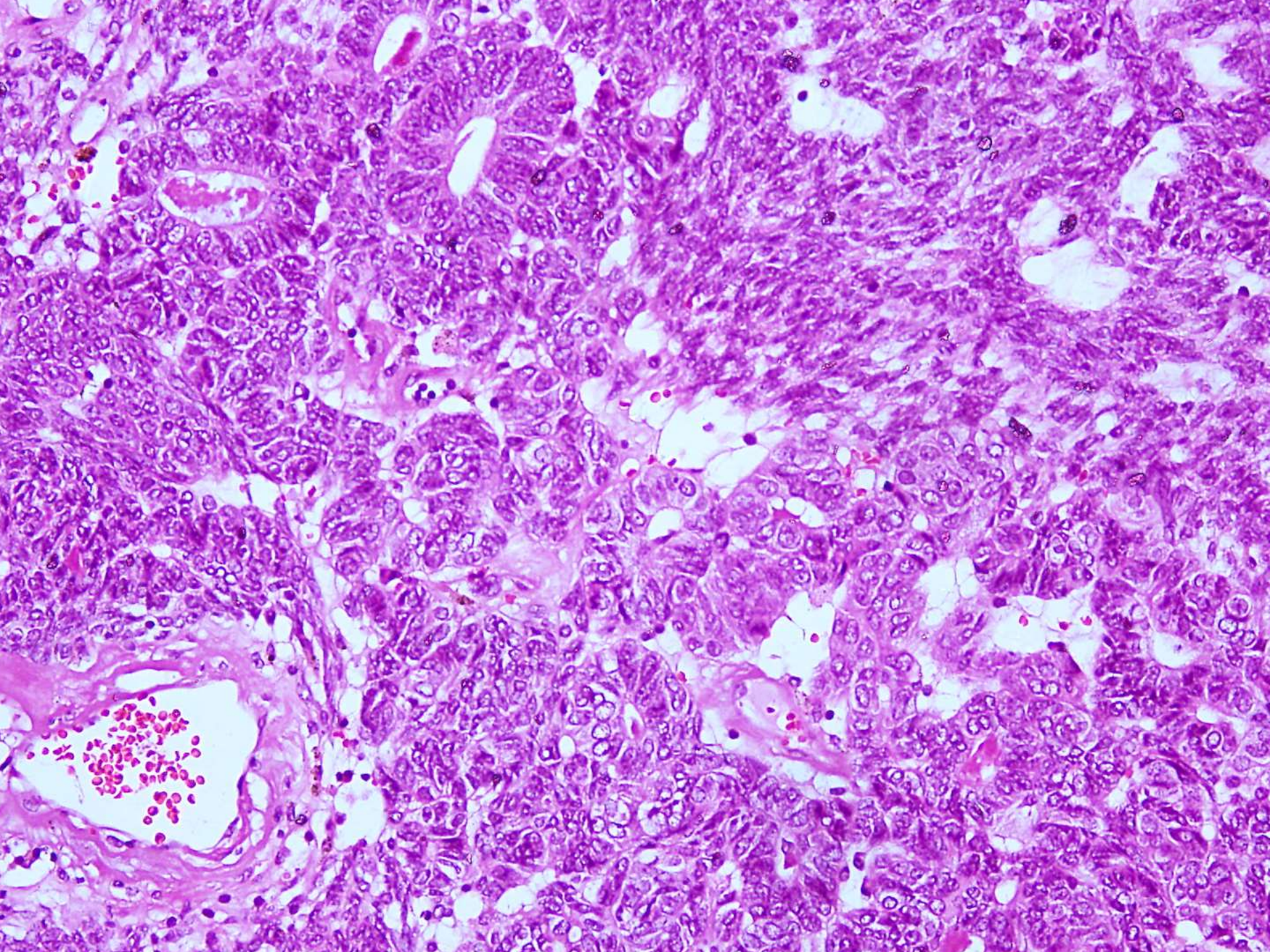
DIAGNOSIS?

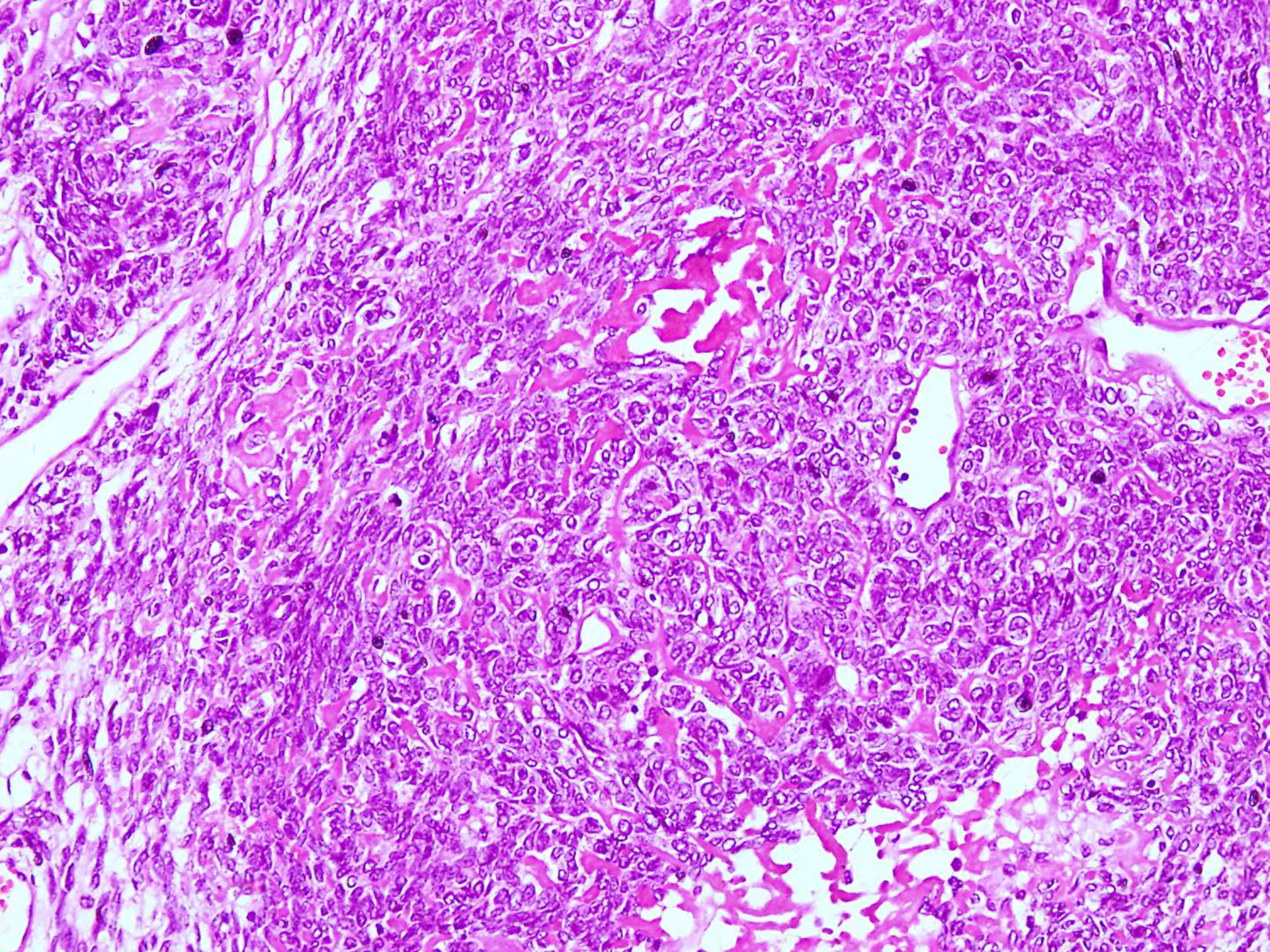


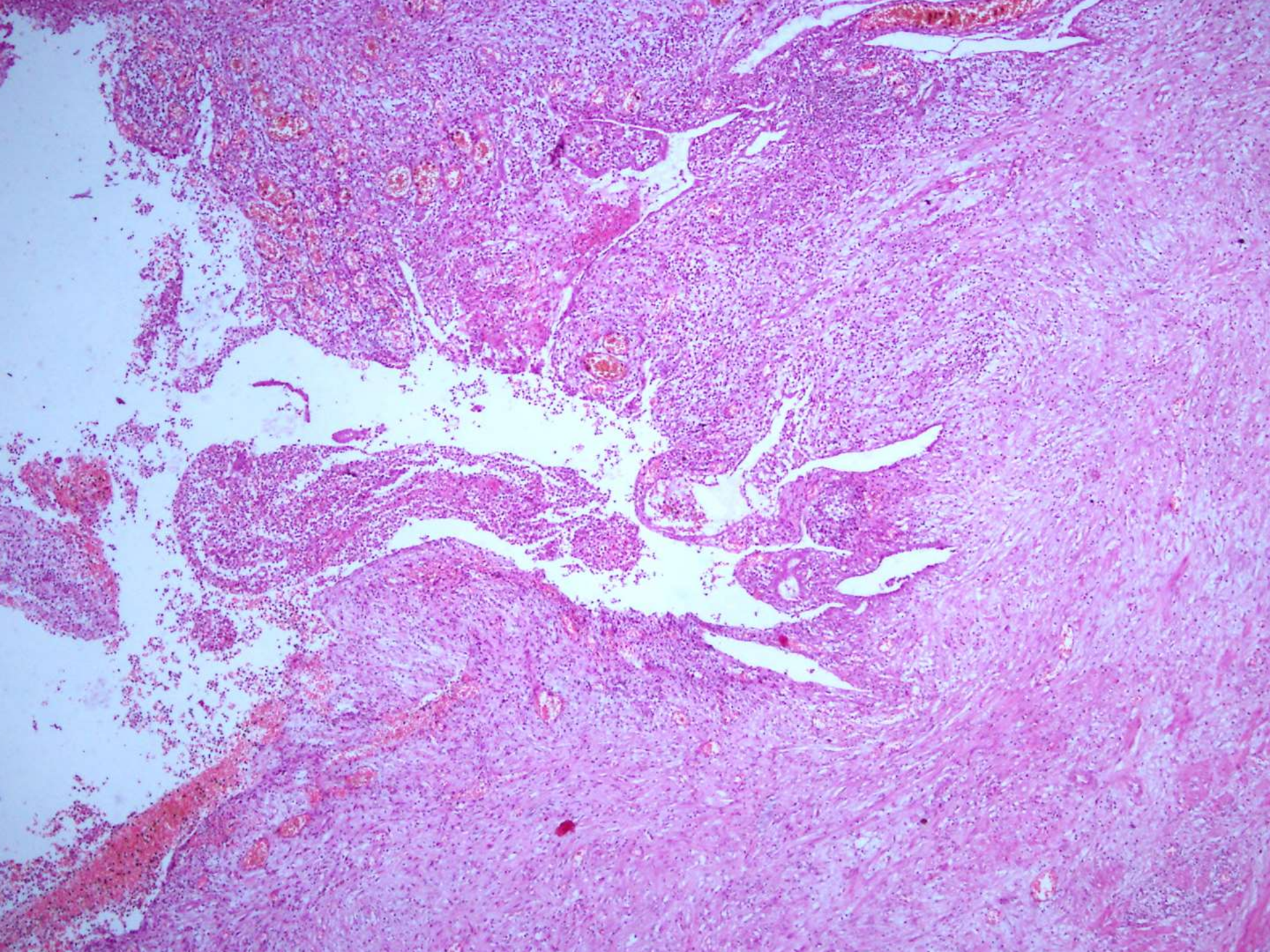


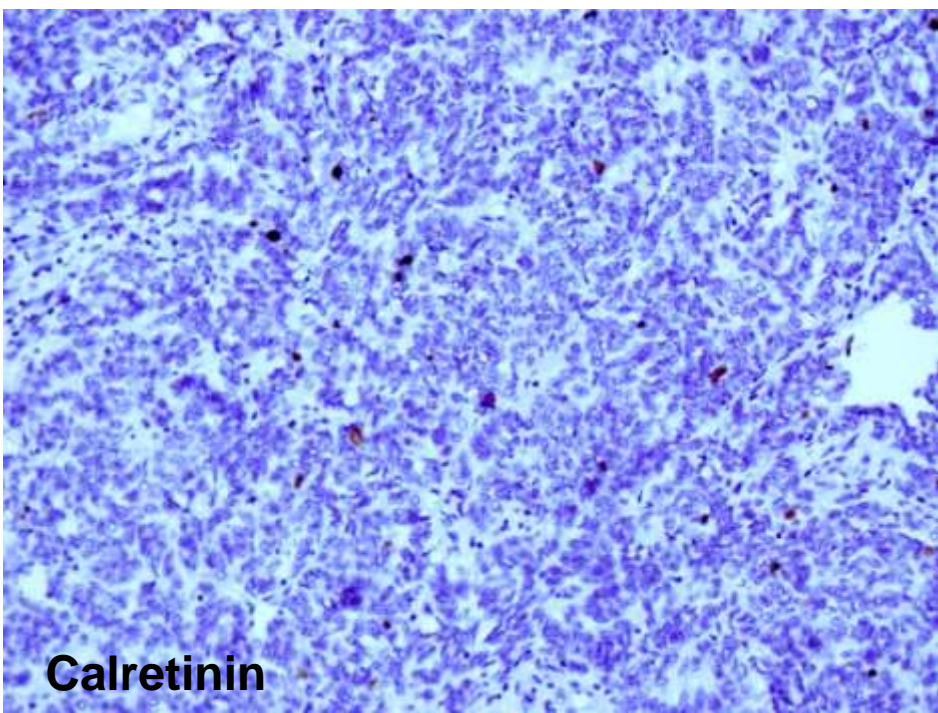
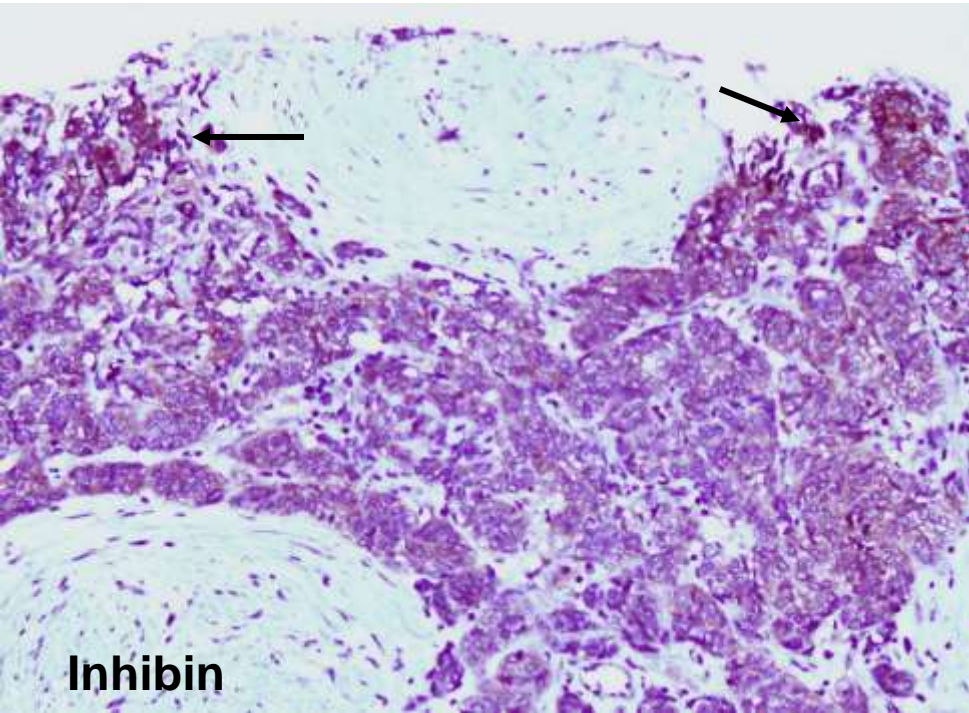
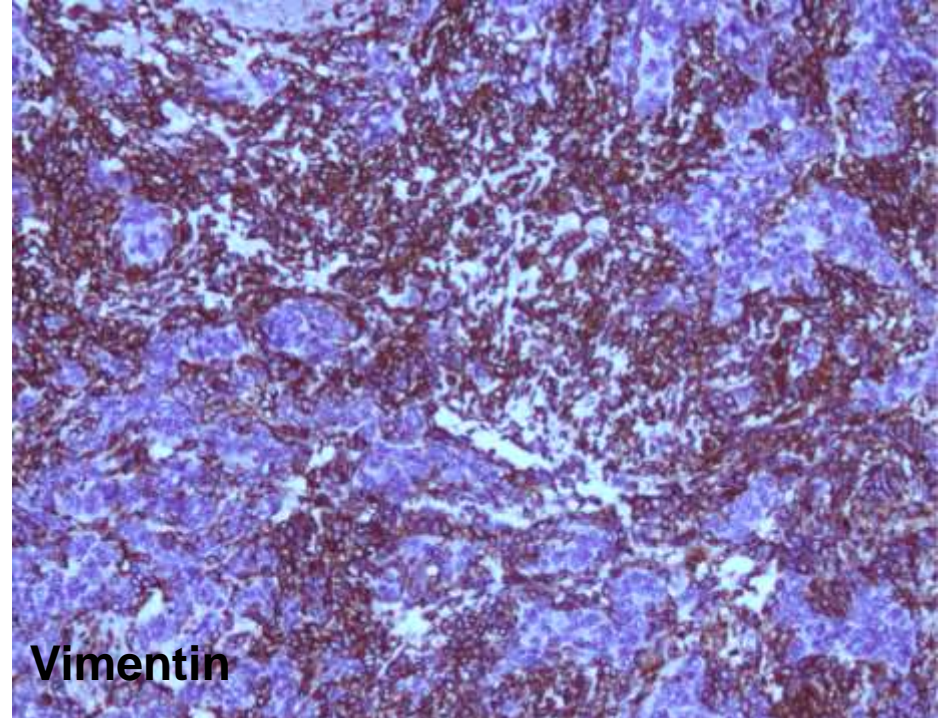
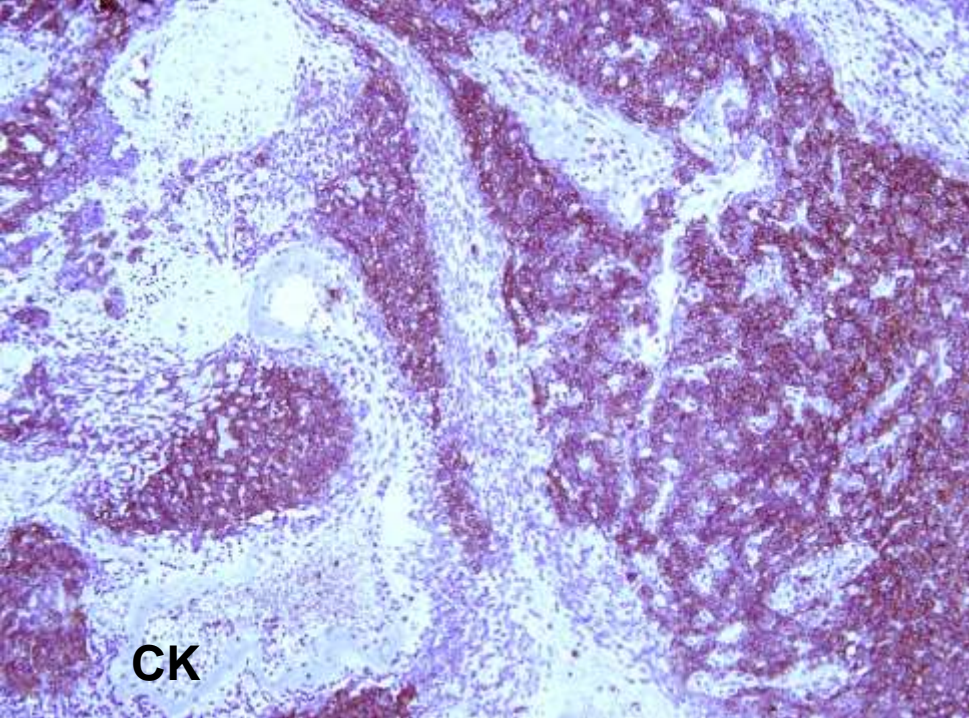


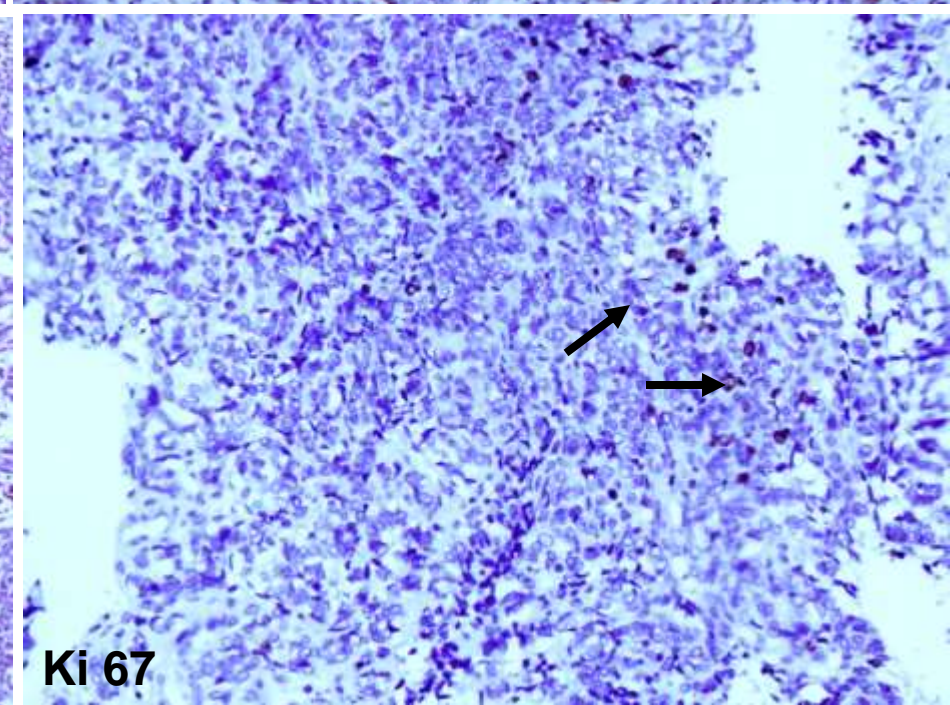
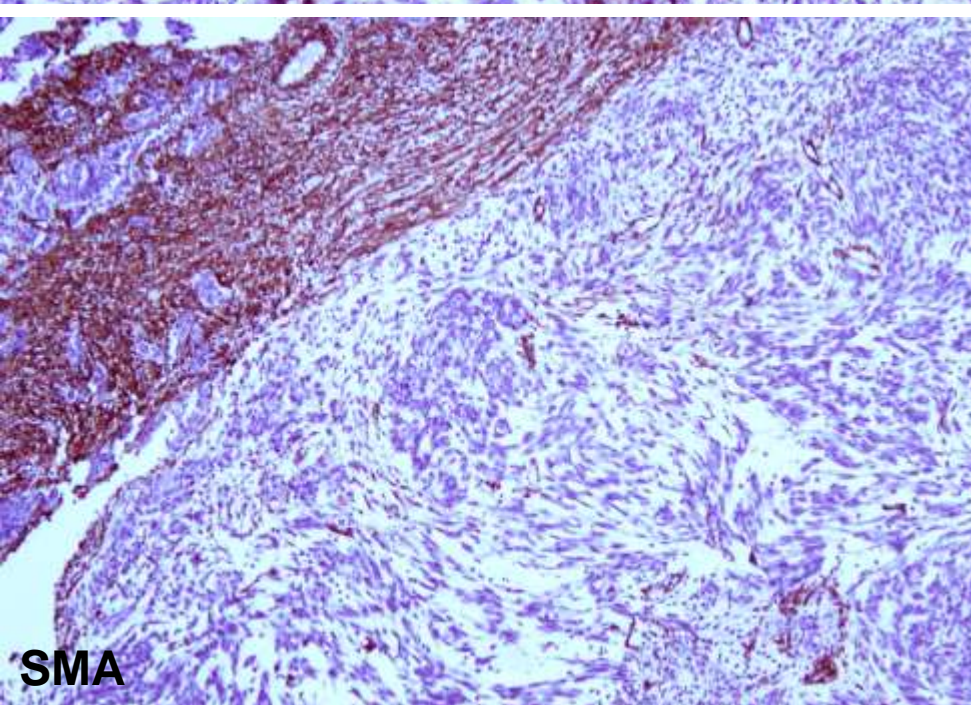
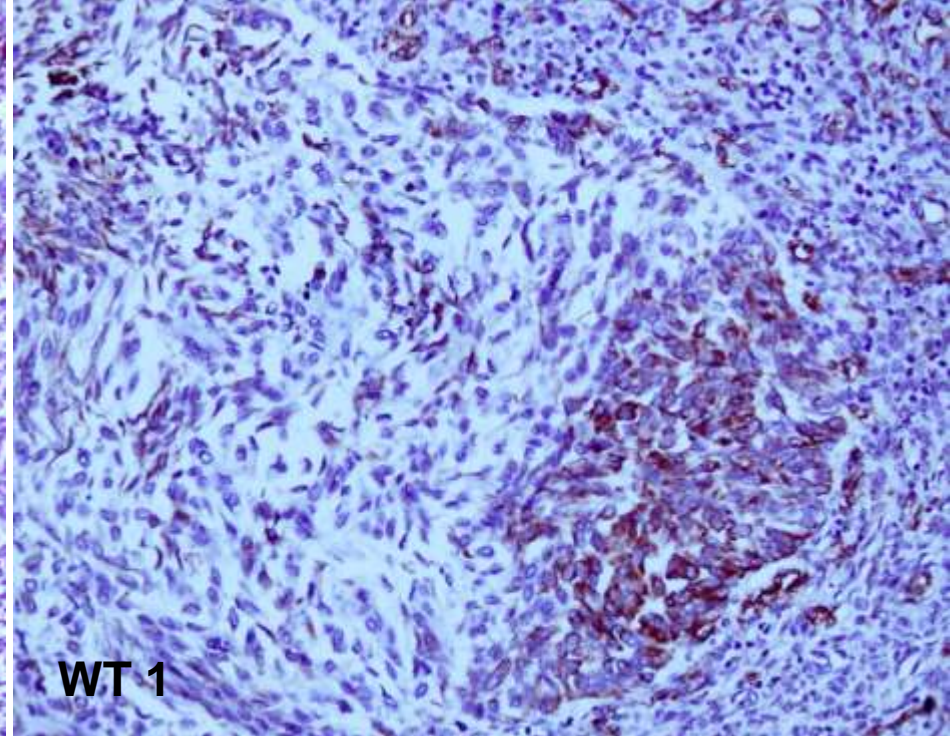
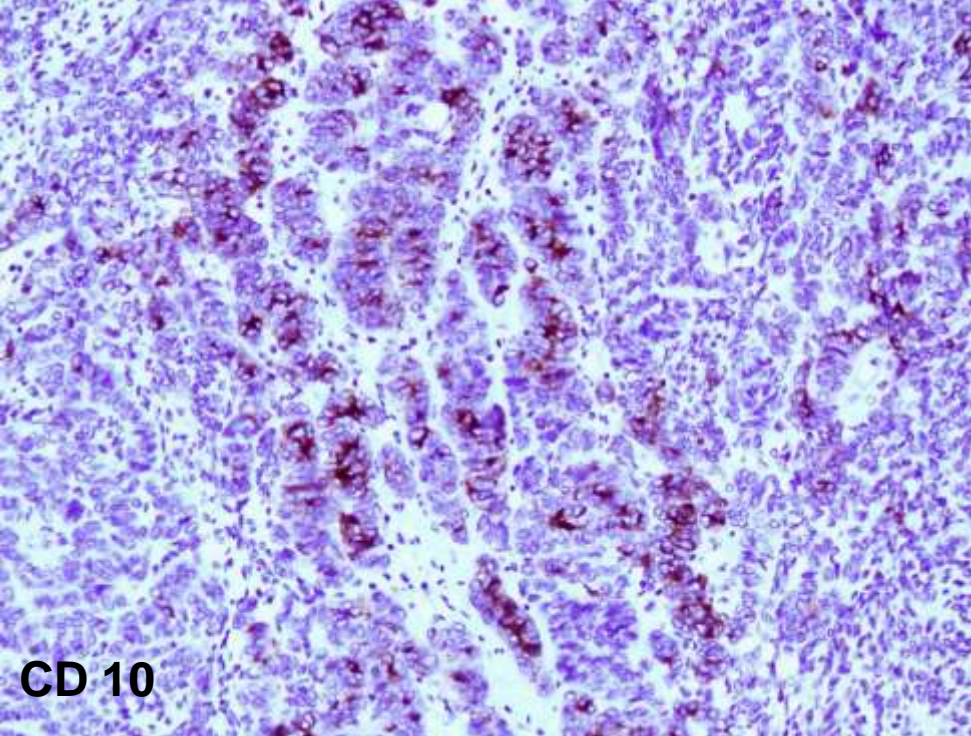












IMMUNOHISTOCHEMICAL PROFILE OF TUMOR

POSITIVE STAINS

Pan CK : 2 to 3 + Epithelial cells
Vimentin : 2 to 3 + Spindle cells & some
Epithelial cells
Inhibin : 1 to 2 +, Focal 5 to 10% cells
Calretinin : 1 to 2 +, Focal 5 to 10% cells
CD 10 : 2 to 3 +, Focal
WT-1 : 2 to 3 +, Focal
SMA : 2 to 3 +, several spindle cells
CD 117 : 1 to 2 +, Focal
EMA : 1 to 2 +, Focal
ER : 2 +, Some epithelial elements
Ki - 67 : 2 to 3 +, in only 2 to 5 % cells

NEGATIVE STAINS

CK 20
CK 7
AFP
CA 125
PAX-8

GROSS: Lumen and wall of left Fallopian tube had a tumor, major part of which was in the mesosalpinx which was removed piece-meal. Left ovary was congested but otherwise normal without tumor.

Right Fallopian tube showed chronic inflammation but no tumor.

The dominant histologic presentation of biphasic epithelial and spindle cell elements in this tumor involving the left fallopian tube and broad ligament merits a differential diagnosis essentially between the following three entities:

- Female Adexal Tumor of probable Wolffian Origin (FATWO)
- Endometrioid carcinoma with prominent spindle cells
- Sertoli-Leydig cell tumor & other SCST

DIAGNOSIS: Female Adnexal Tumor of probable Wolffian Origin (FATWO)

- IHC profile closely akin to that of Wolffian (Mesonephric) duct remnants like Rete Ovarii
- Morphologic and cytologic features suggest low malignant potential (unlike Endometrioid carcinoma)
- PAX -8 -ve (Endometrioid Ca Pax-8 +ve)*
- Inhibin and WT-1 only focal +ve (unlike SCSTs**)

Diffuse CD117 +vity of FATWO may be associated with favourable response to Rx with Tyrosin Kinase Inhibitor***

•*Int J Gynecol Pathol 2016,35:167-75

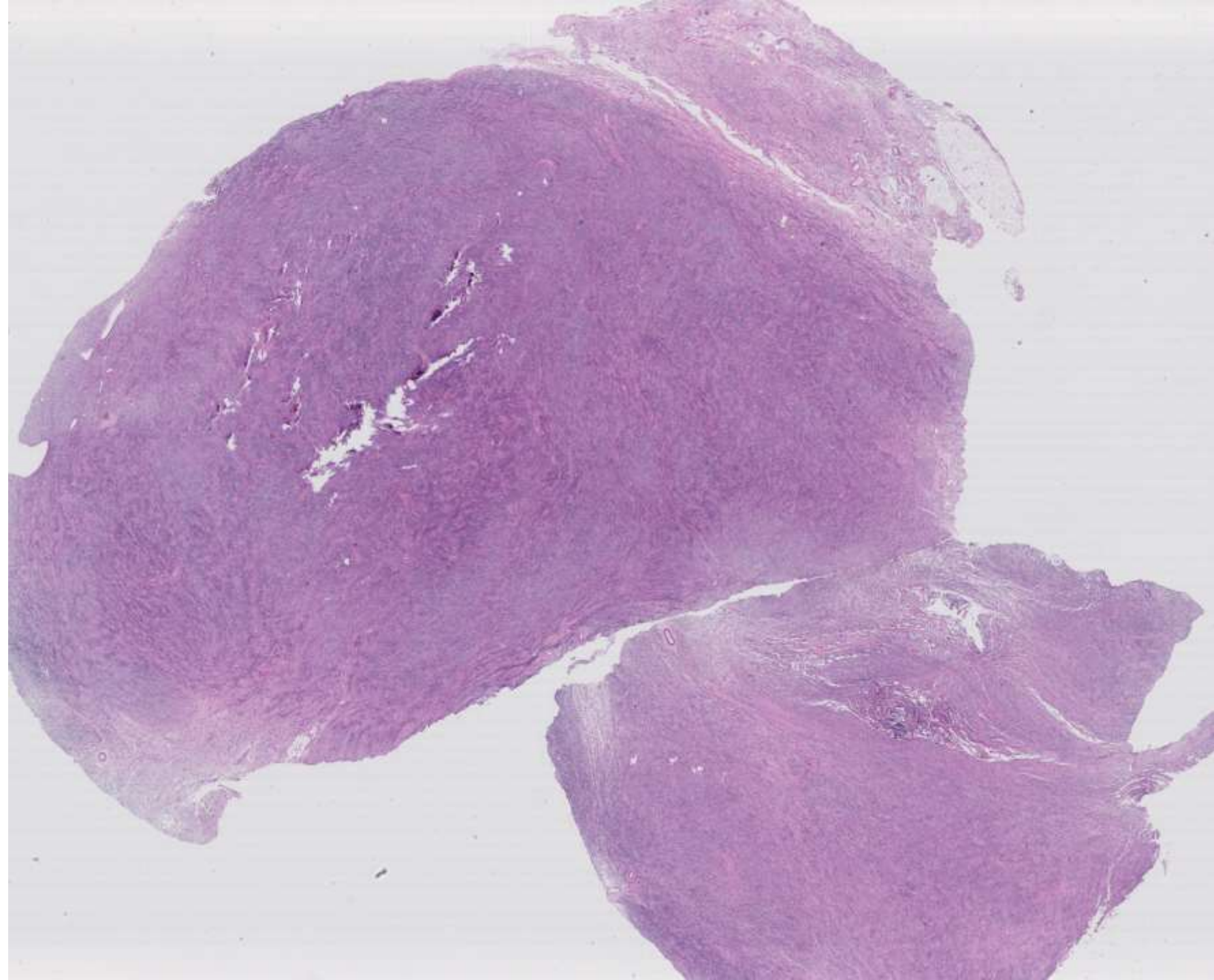
•**Amer J Surg Path 2009,33: 354-66

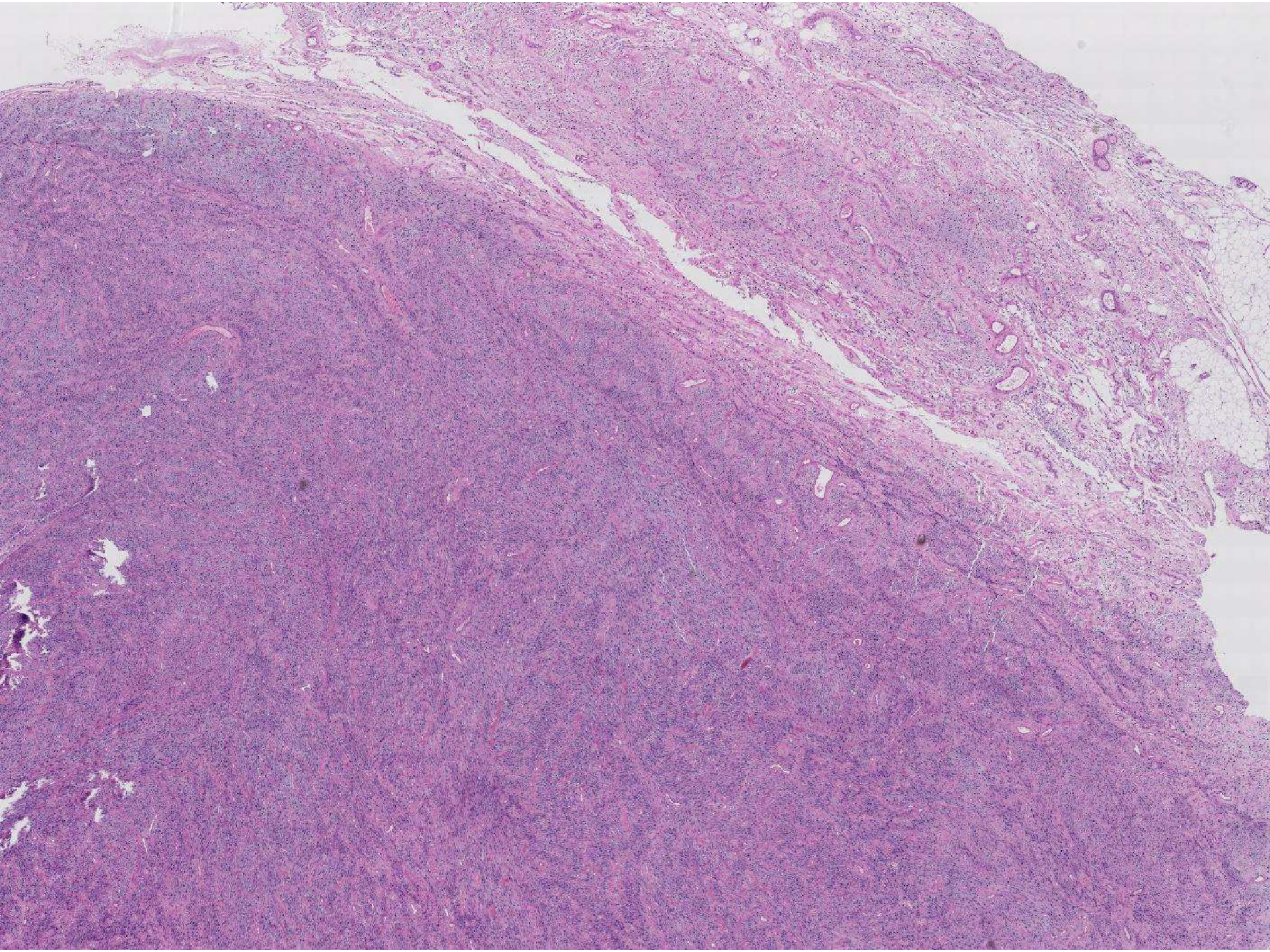
•***Human Pathol doi.10.1016/j.jehc.2015.05.006

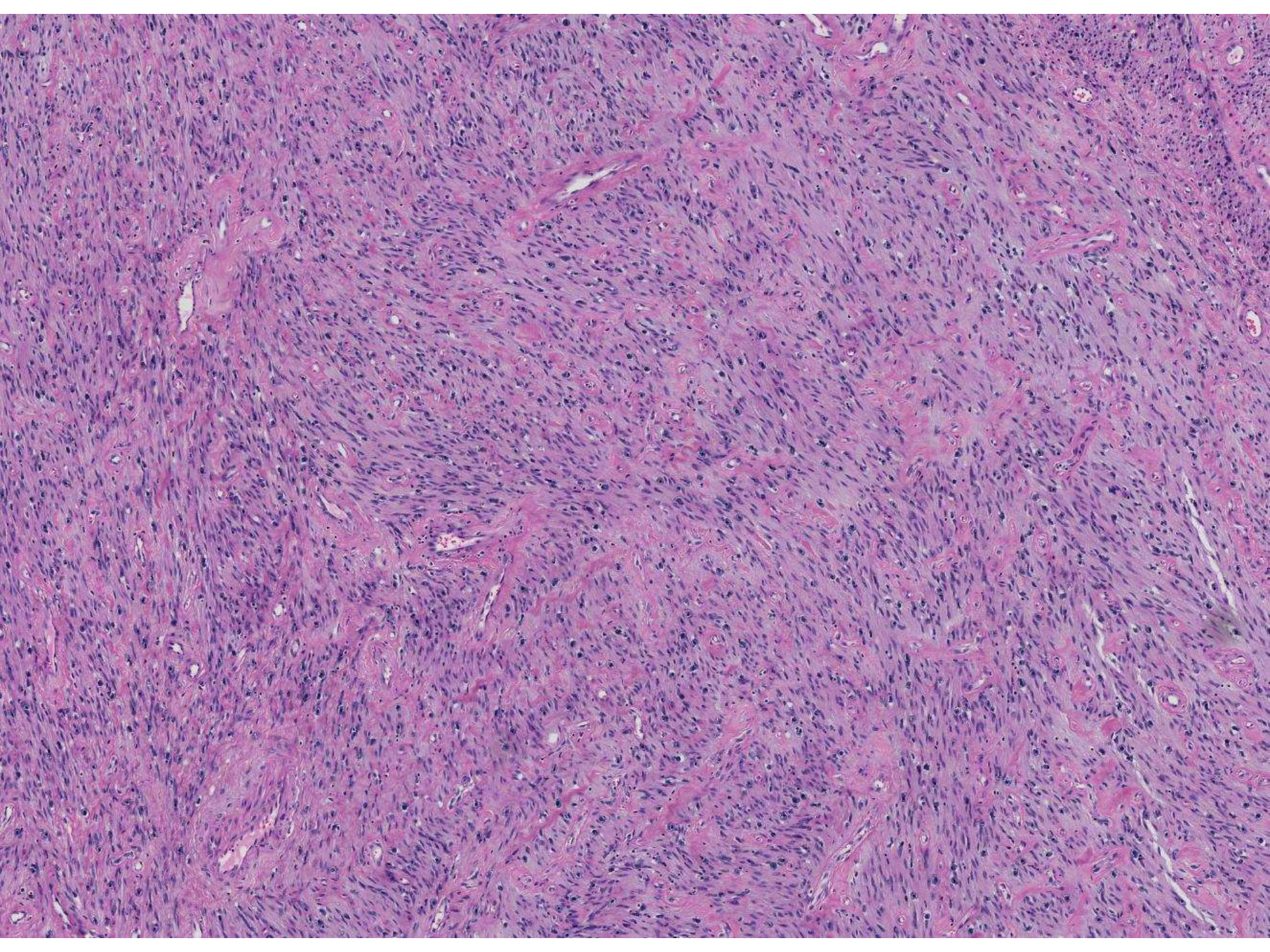
SB 6047

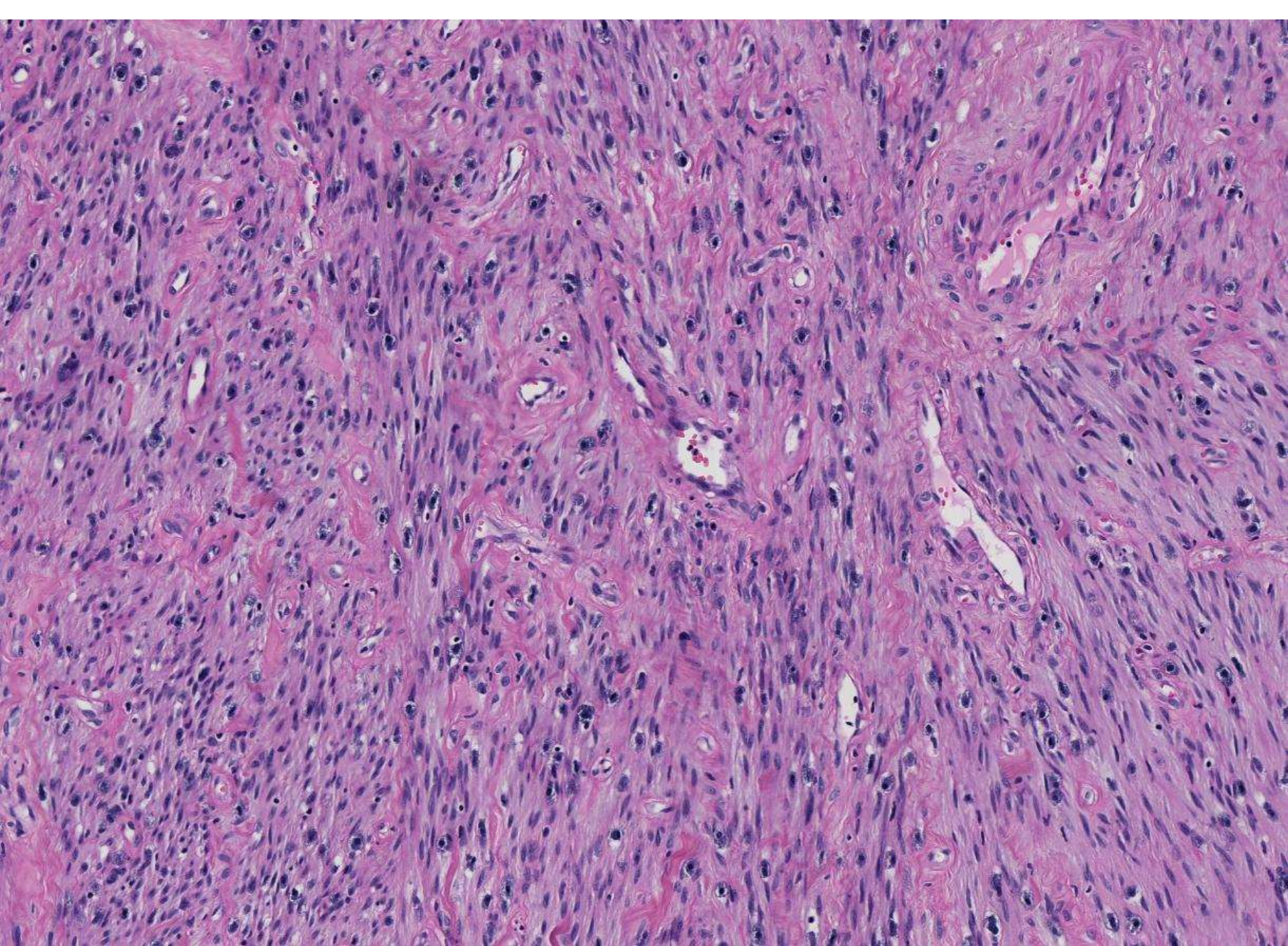
Caroline Temmins; Santa Clara Valley Medical Center

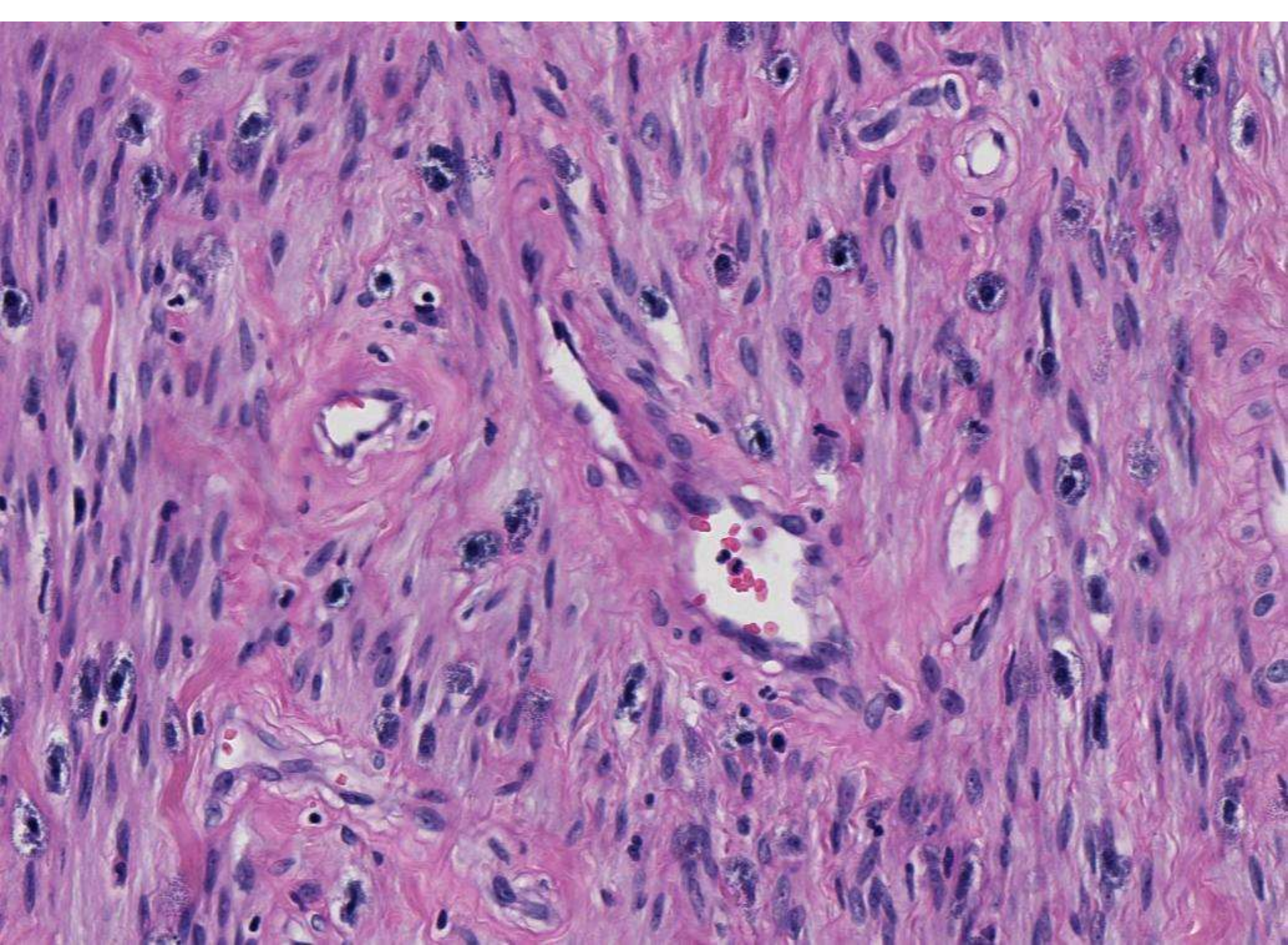
57-year-old man with history of >20cm right scrotal mass, growing for 7 years, thought to be paratesticular tumor. Underwent right radical orchiectomy/hemiscrotectomy.

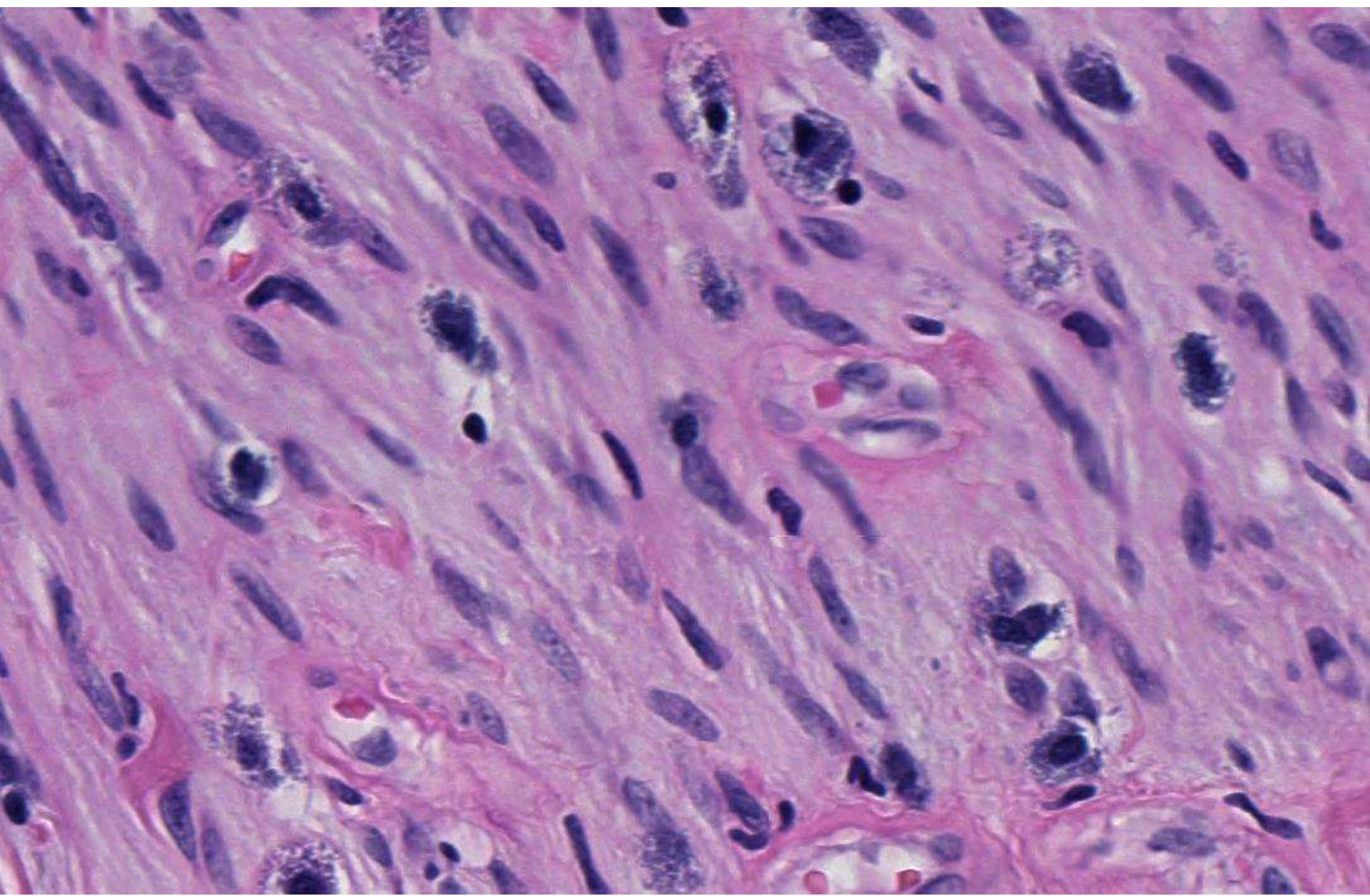


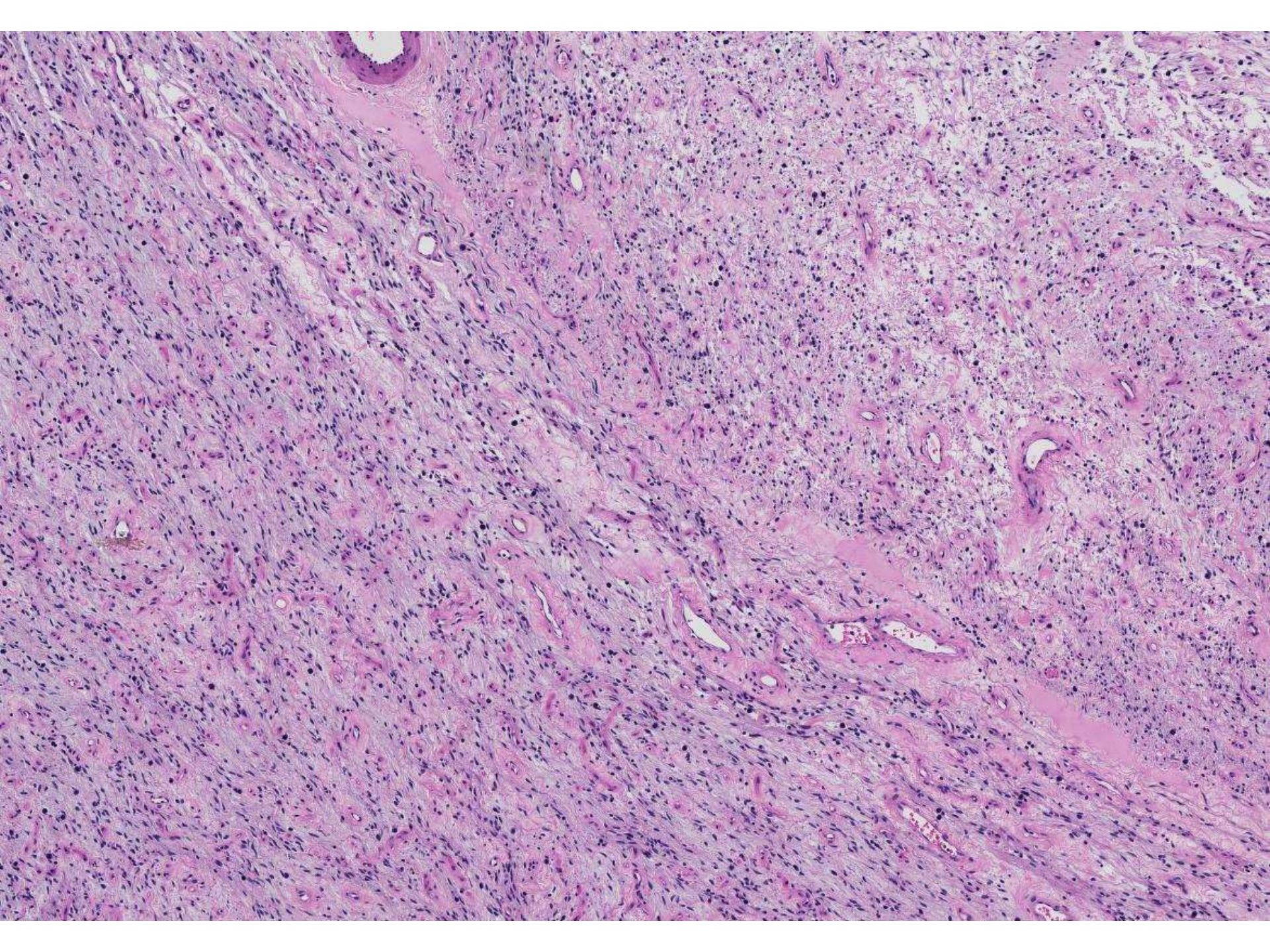


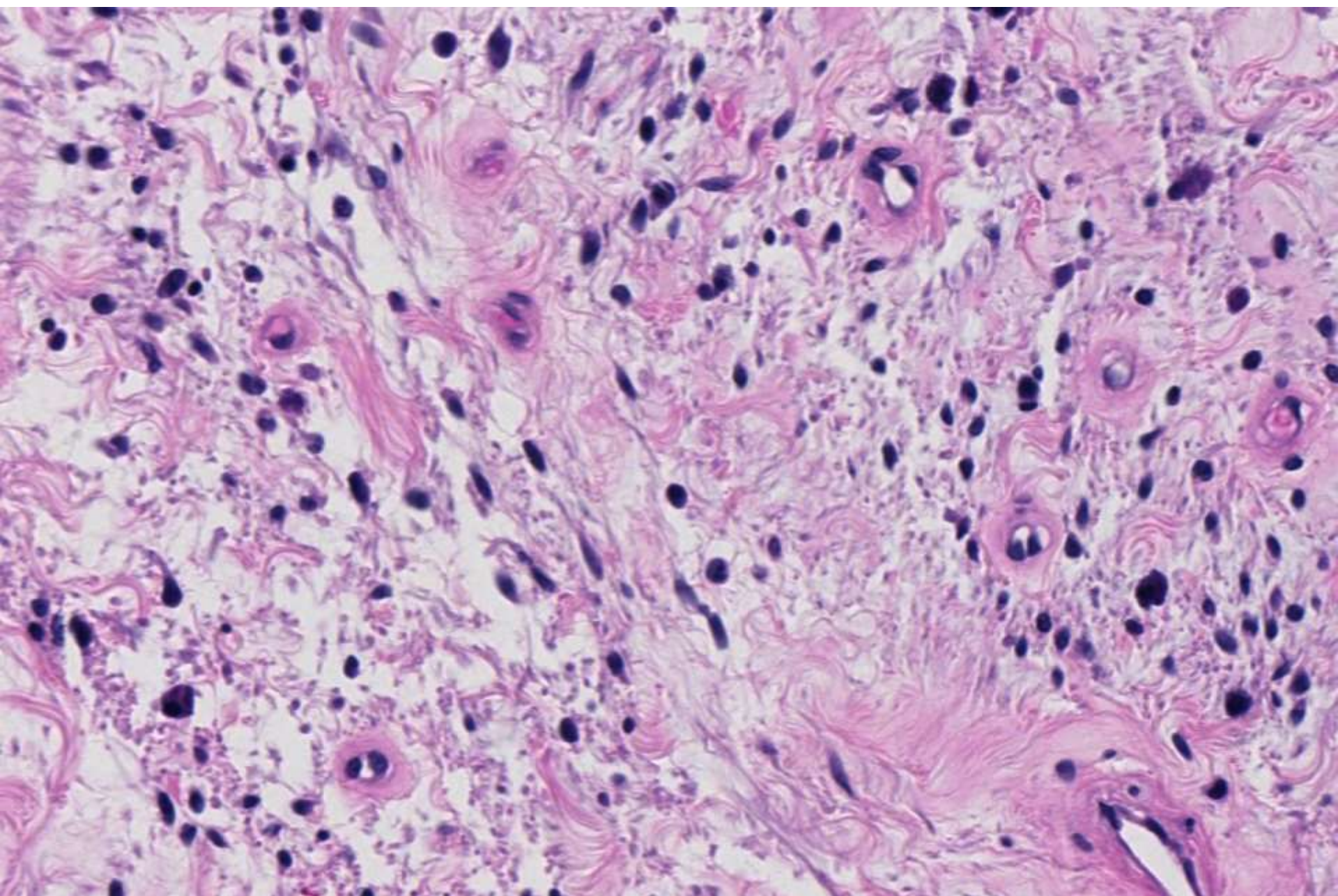


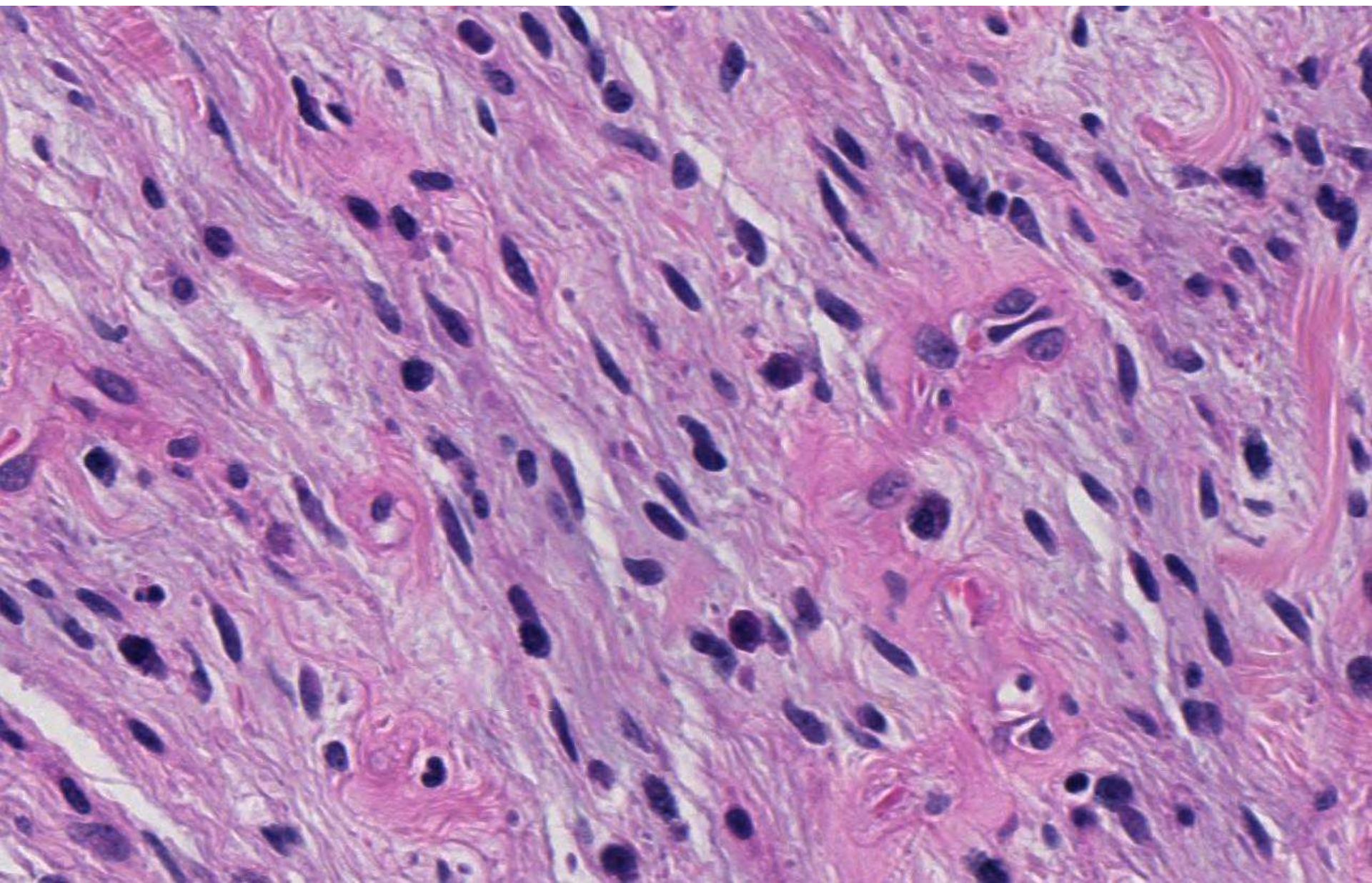




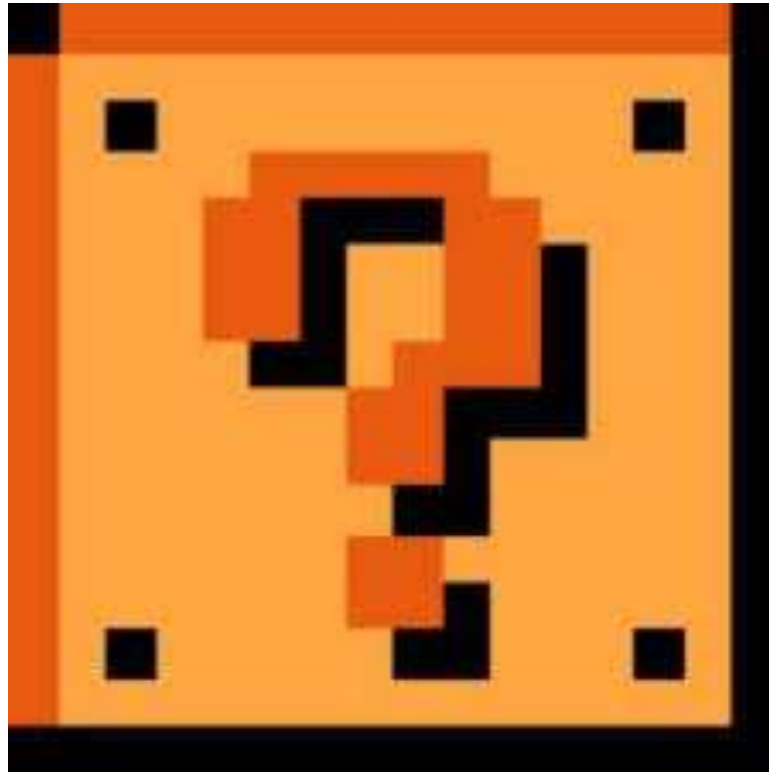




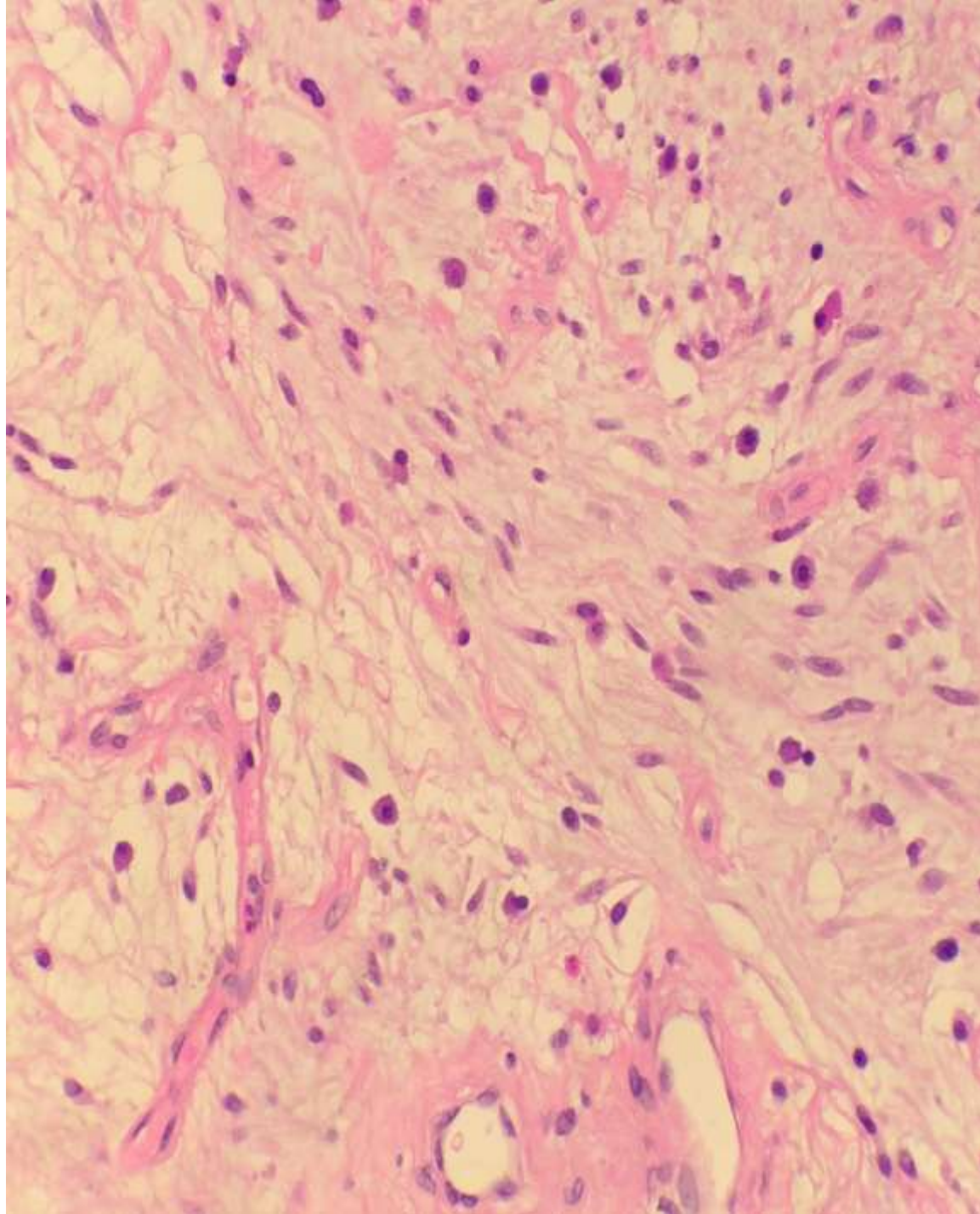


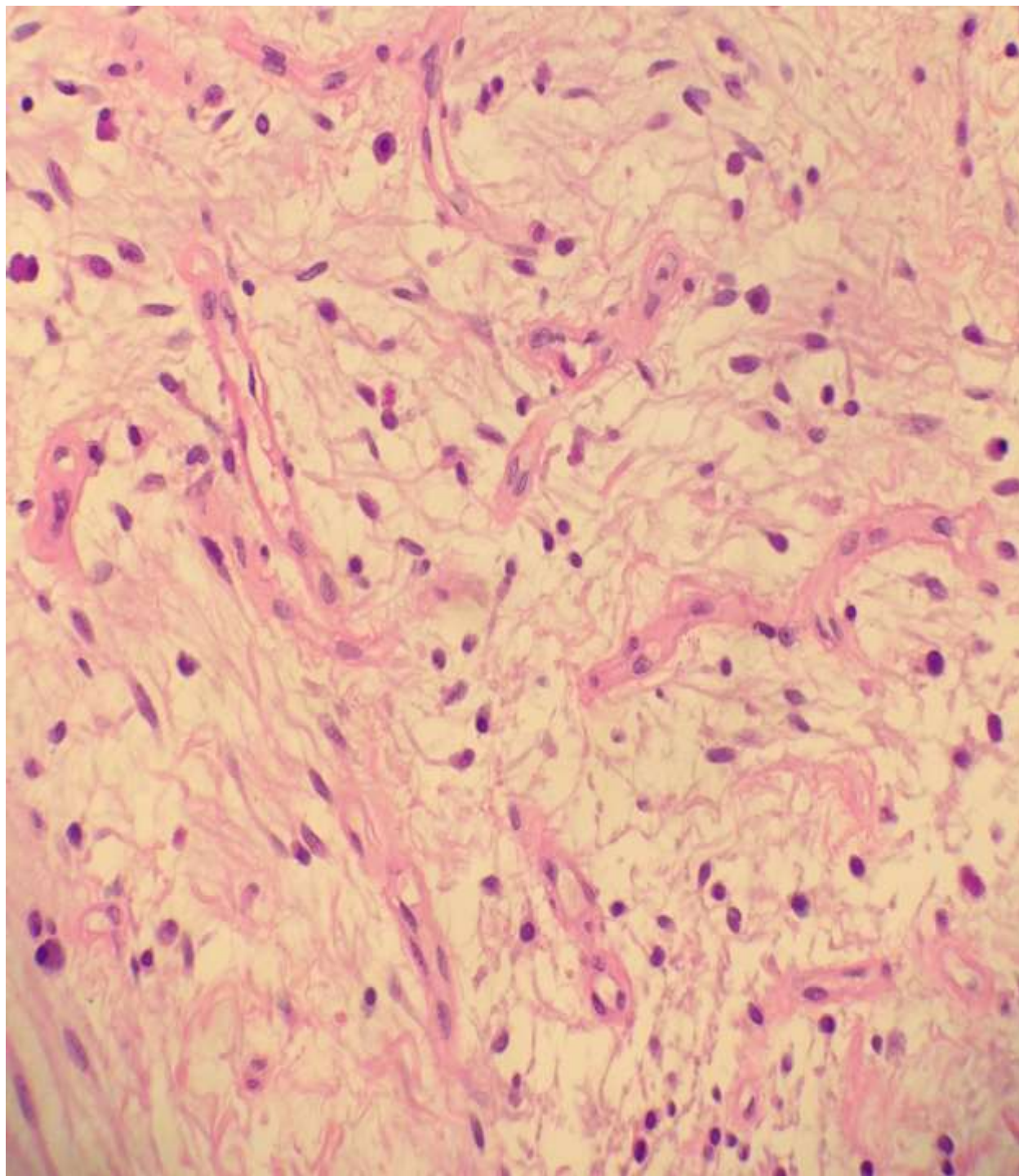


DIAGNOSIS?



- 58 year old man, presented to the ER with Zoster, noted to have a scrotal mass, first noted by patient 7 years ago.
- U/S showed right paratesticular mass, extending from the peritoneum to the level of the knees.
- Testicle and spermatic cord removed – no tumor. Seminiferous tubules with sertoli-only pattern.
- Right paratesticular mass: 22 x 20 x 10 cm, 3,600 grams lobulated yellow-red soft tissue. Lobulated yellow fatty cut surface with focal areas of hemorrhage.

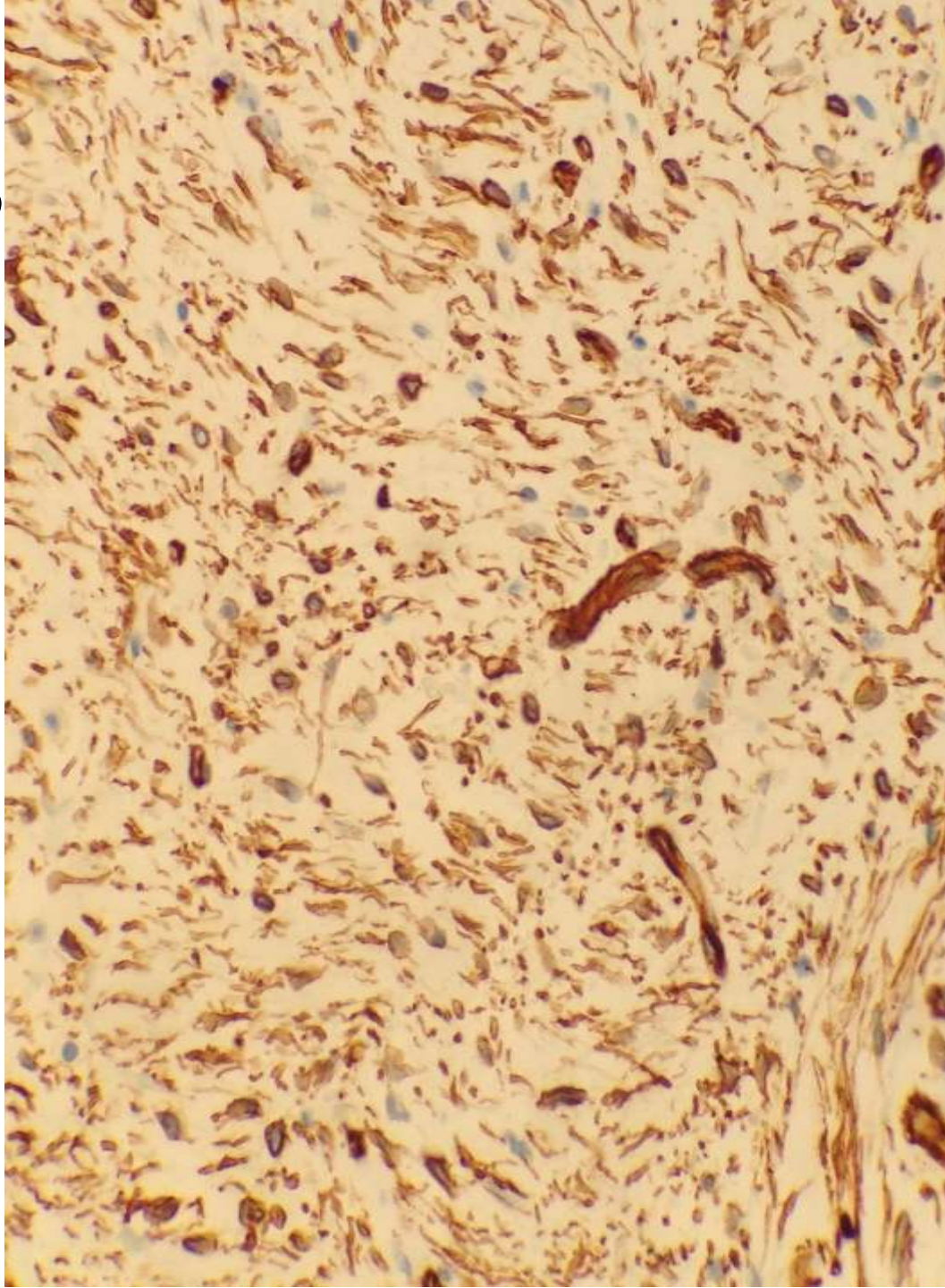




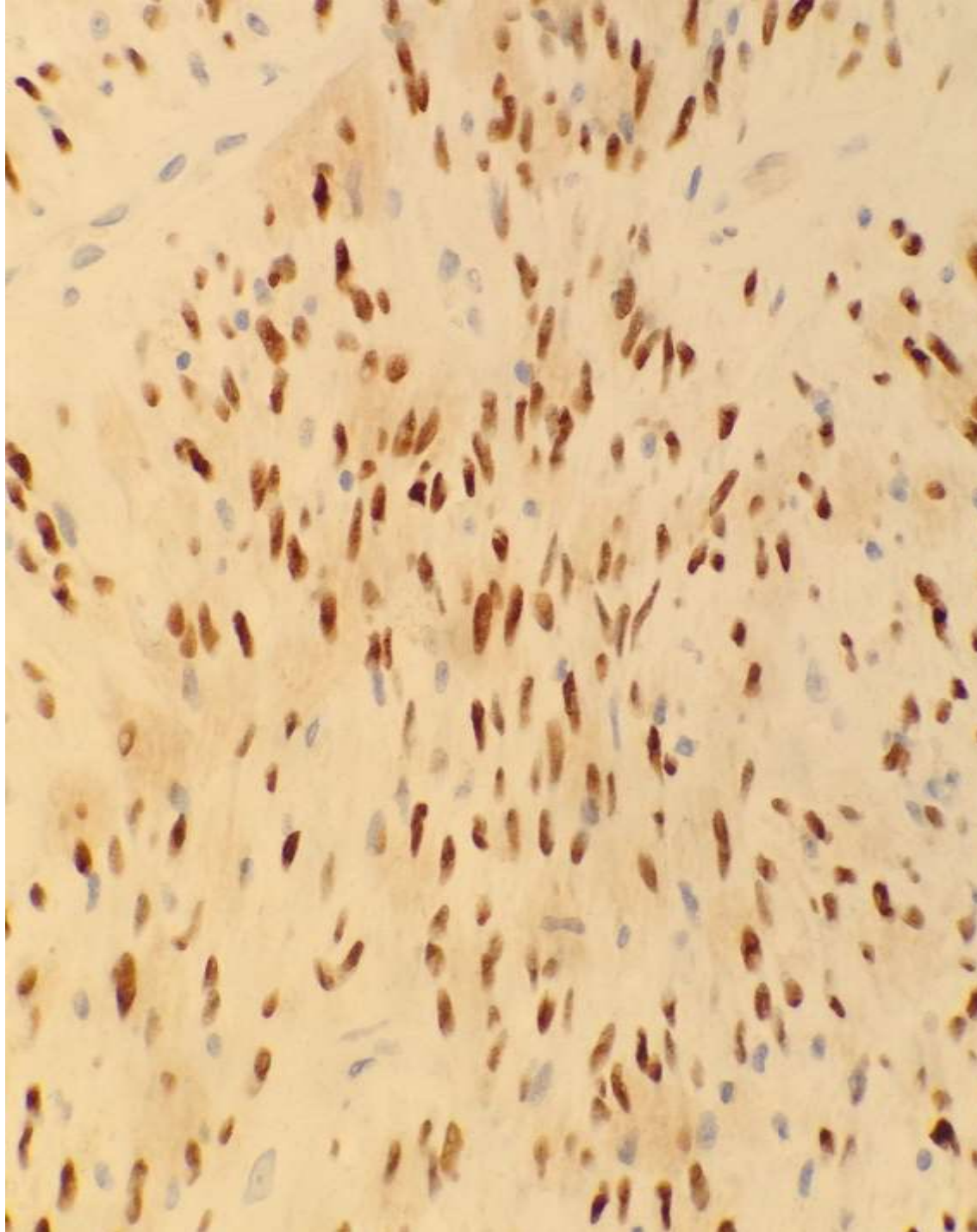
DDx:

- Cellular angiofibroma (angiomyofibroblastoma-like tumor of the male genital tract)
- Dedifferentiated liposarcoma
- Nerve sheath tumor
- Other mesenchymal neoplasm

CD3



ER



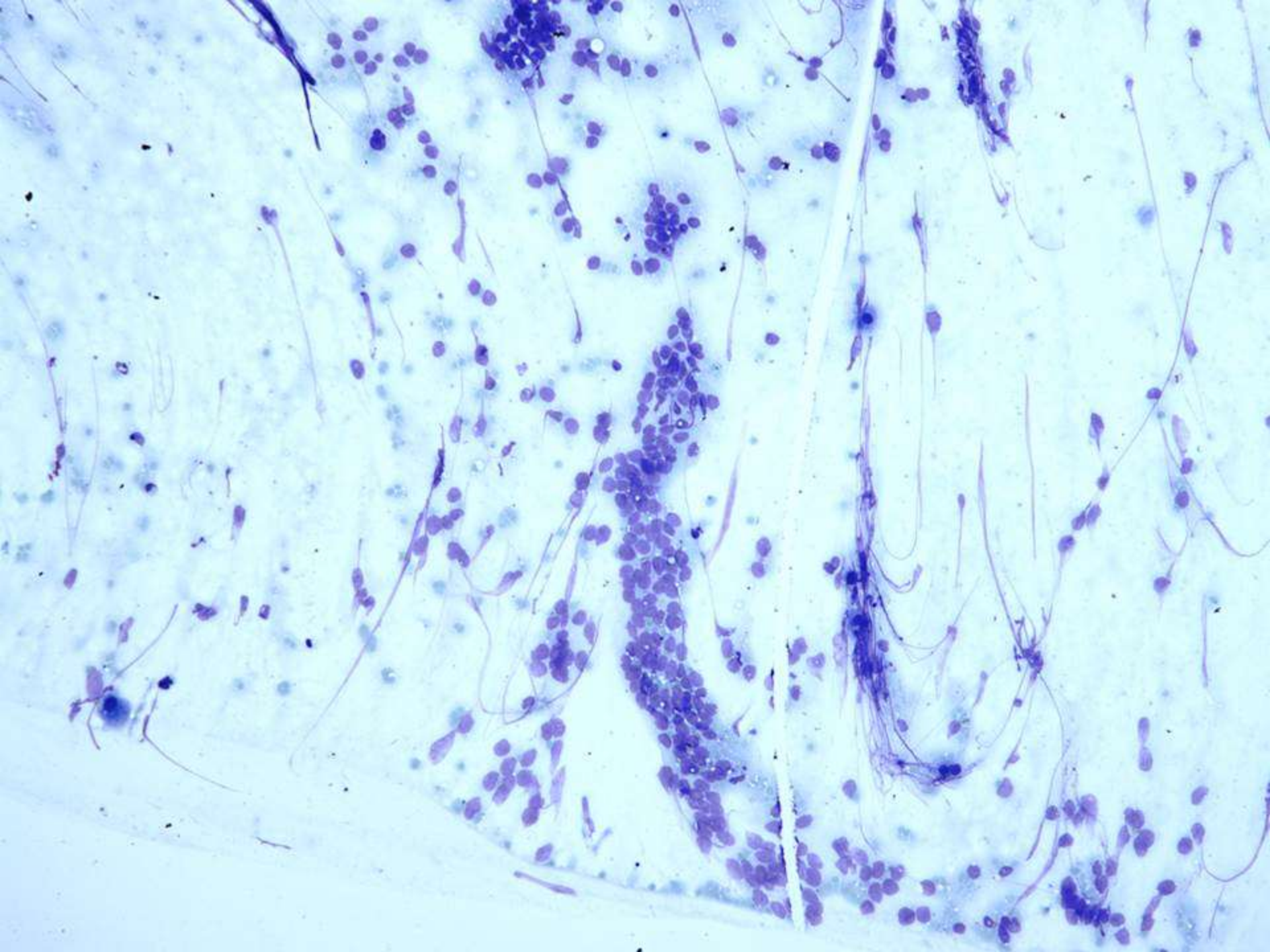
- Vimentin
 - ER
 - Actin (weak)
 - CD34
-
- Negative stains: Calretinin, MOC-31, S100, cytokeratin AE1/AE3, desmin, PR
-
- Performed at UCSF:
 - Rb – negative in tumor cells, positive in endothelial cells and mast cells
 - MDM2: negative
 - CDK4: negative
 - SOX10: negative

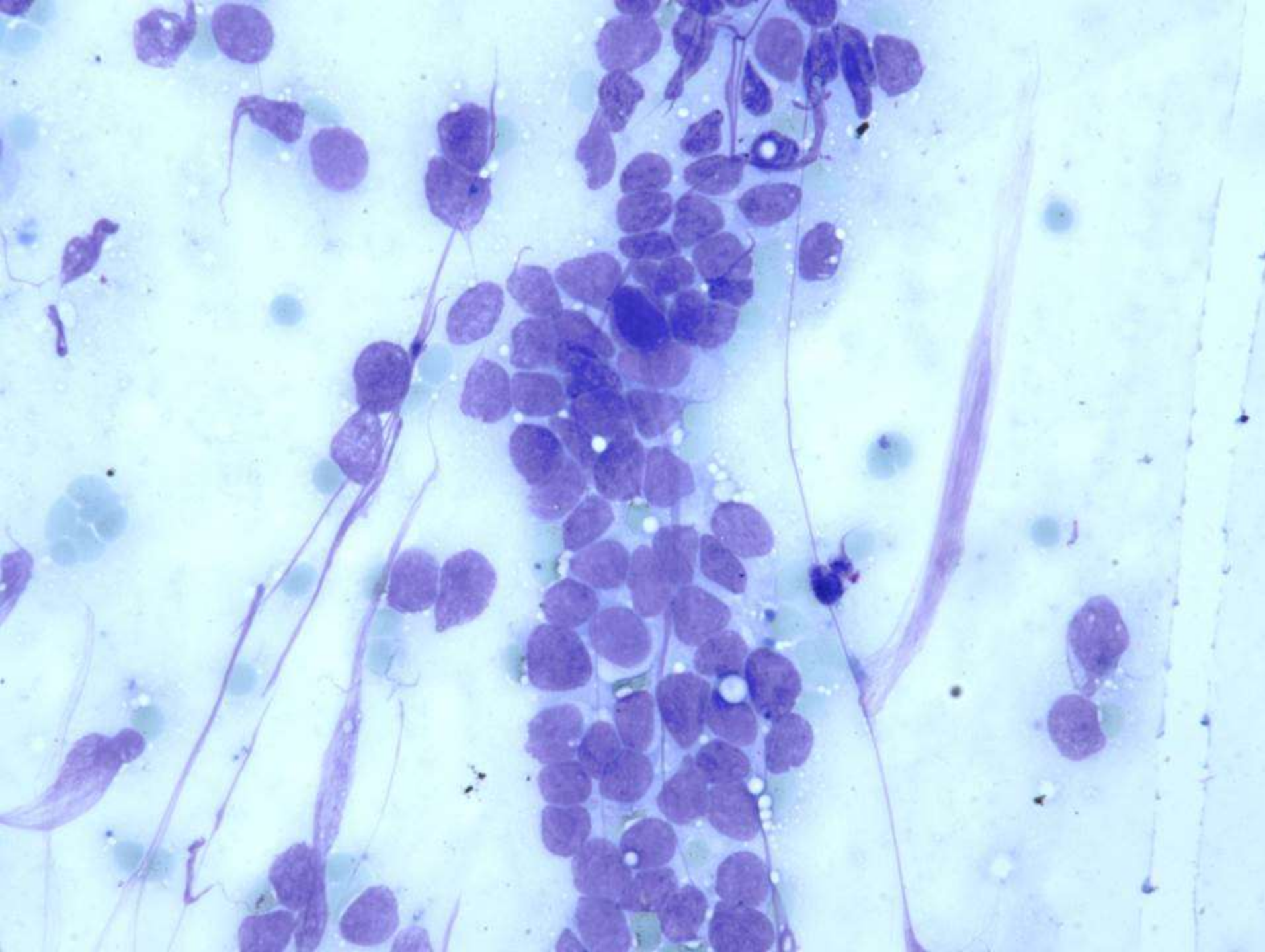
Cellular angiofibroma (angiomyoibroblastoma-like tumor of the male genital tract)

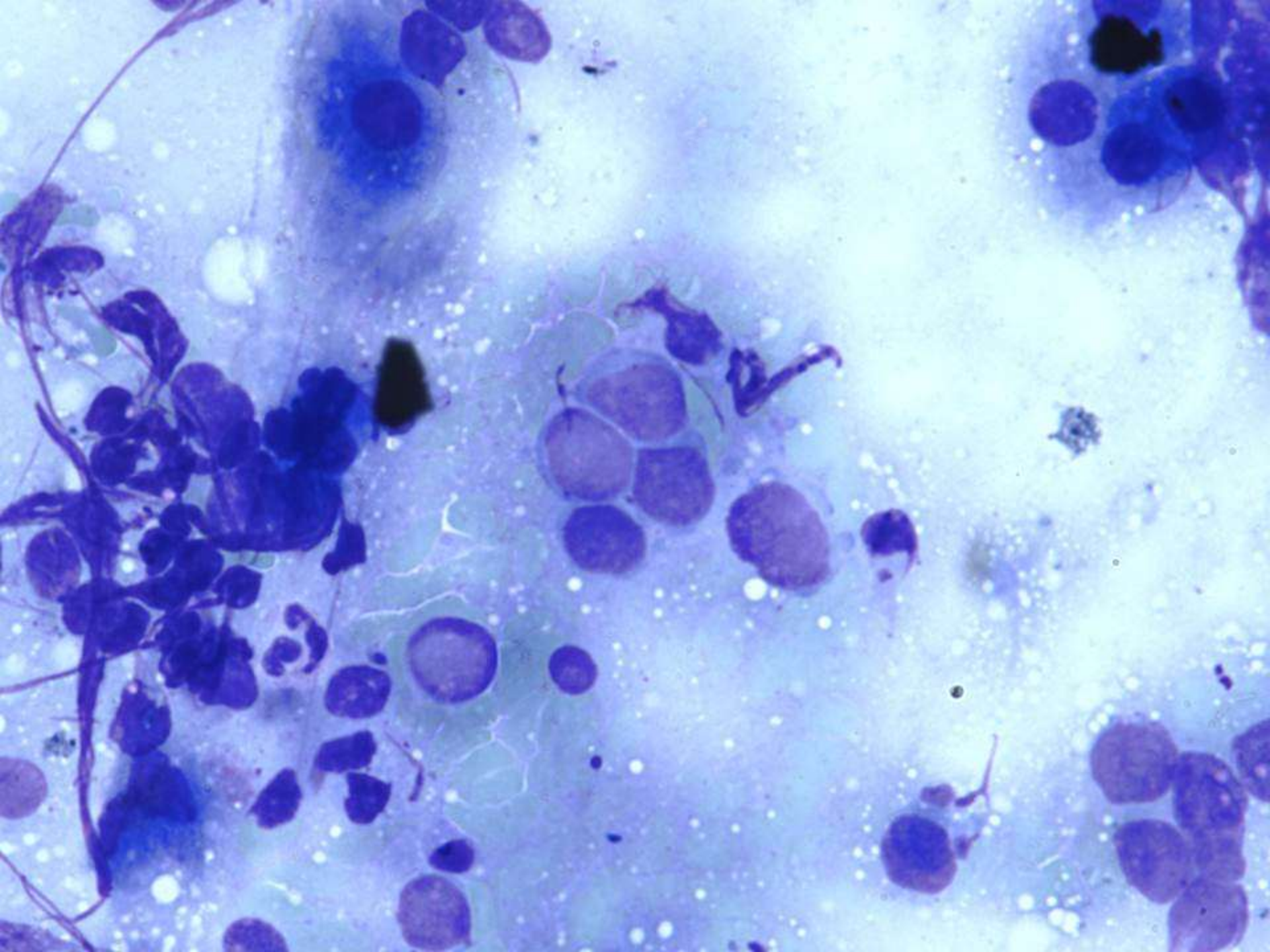
- Restricted to external genitalia and perineal soft tissue
 - Rare in males
- Most under 5 cm
- Circumscribed with thin pseudocapsule
- Edematous background with prominent vascularity
 - Thin walled dilated capillaries and venules
 - Scattered bundles of collagen
 - Occasionally sclerotic
 - No necrosis
- Alternating hypercellular and hypocellular areas

SB 6048

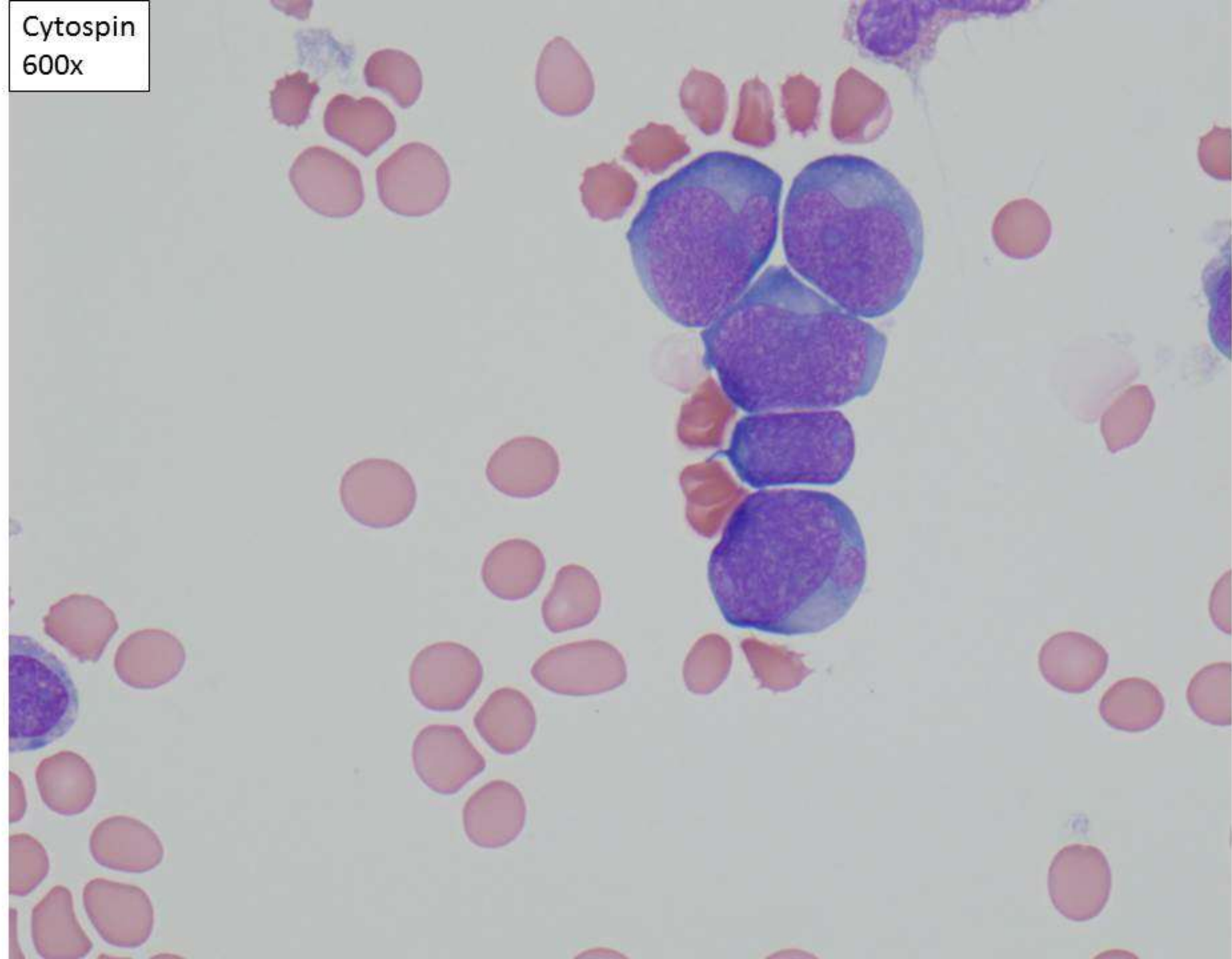
Sebastian Fernandez-Pol/Robert Ohgami; Stanford
66-year-old male with innumerable liver lesions, FNA
submitted.



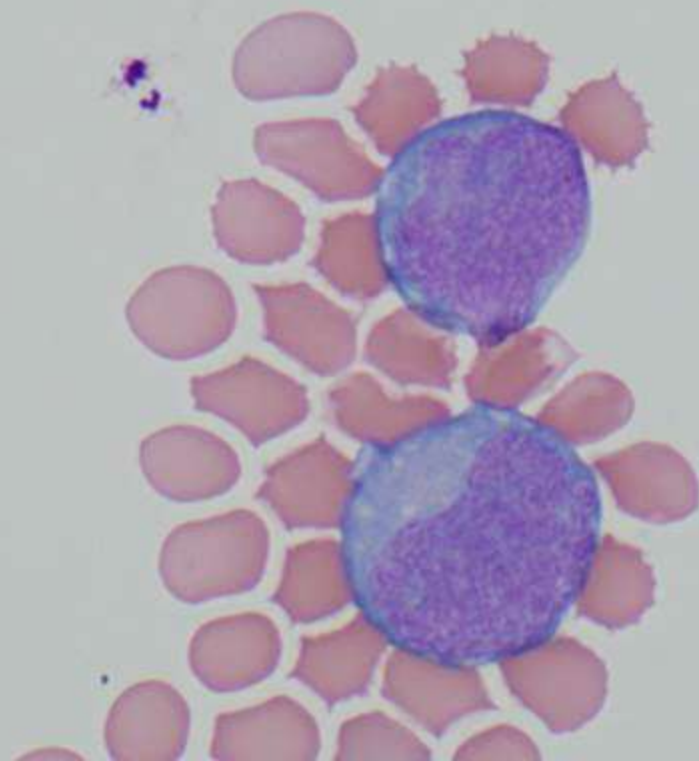


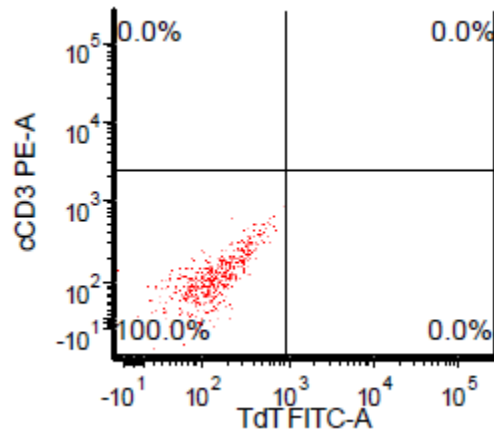
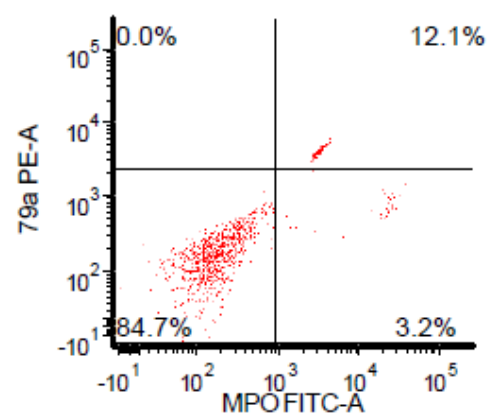
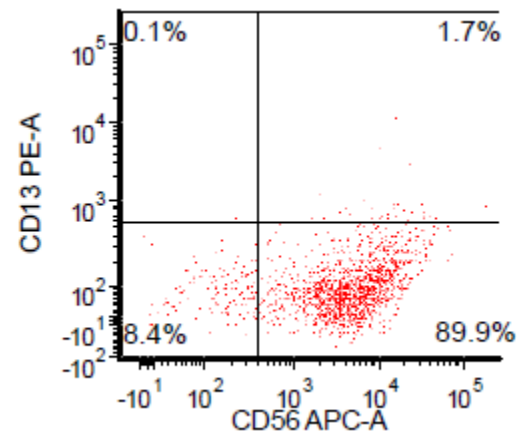
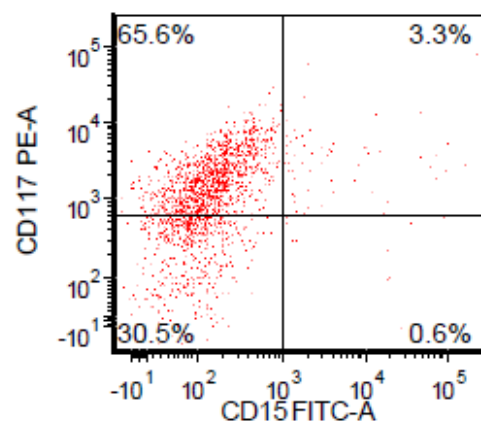
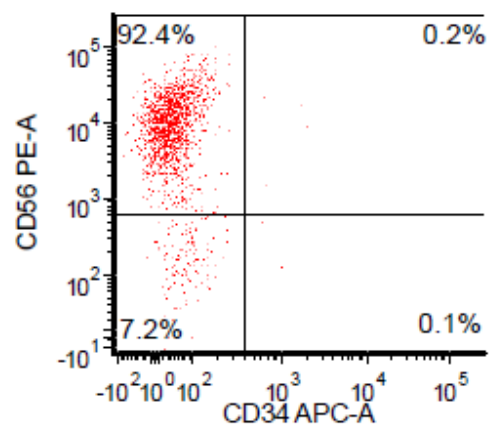
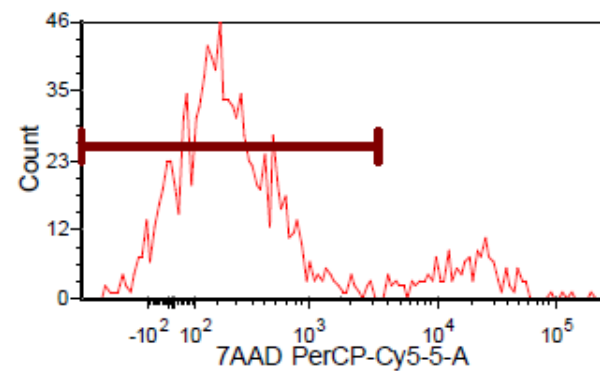
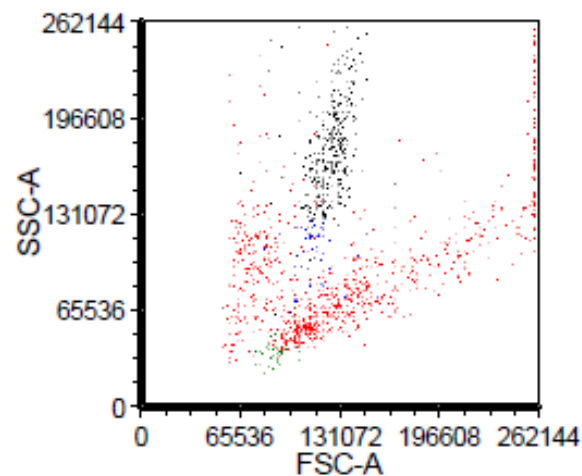
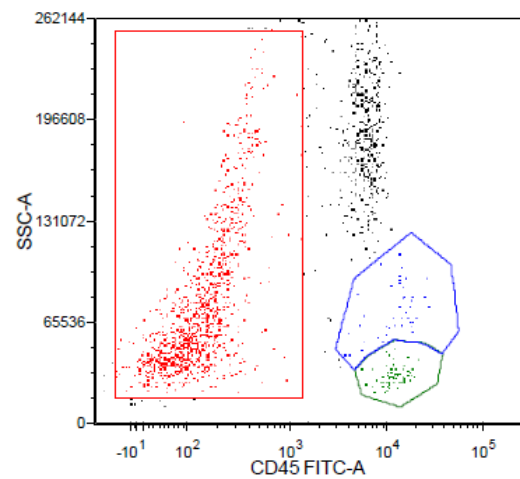


Cytospin
600x

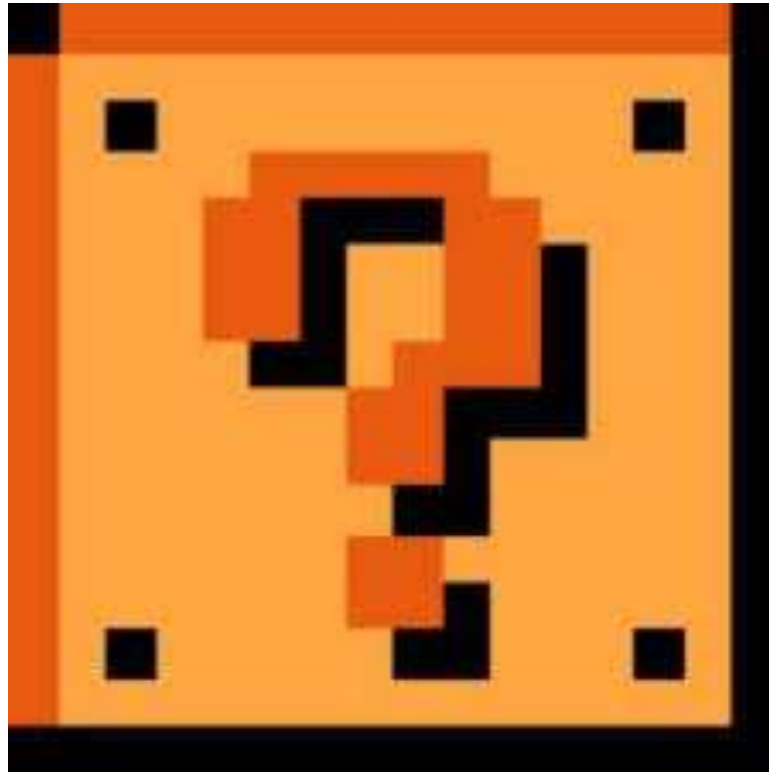


Cytospin
600x





DIAGNOSIS?

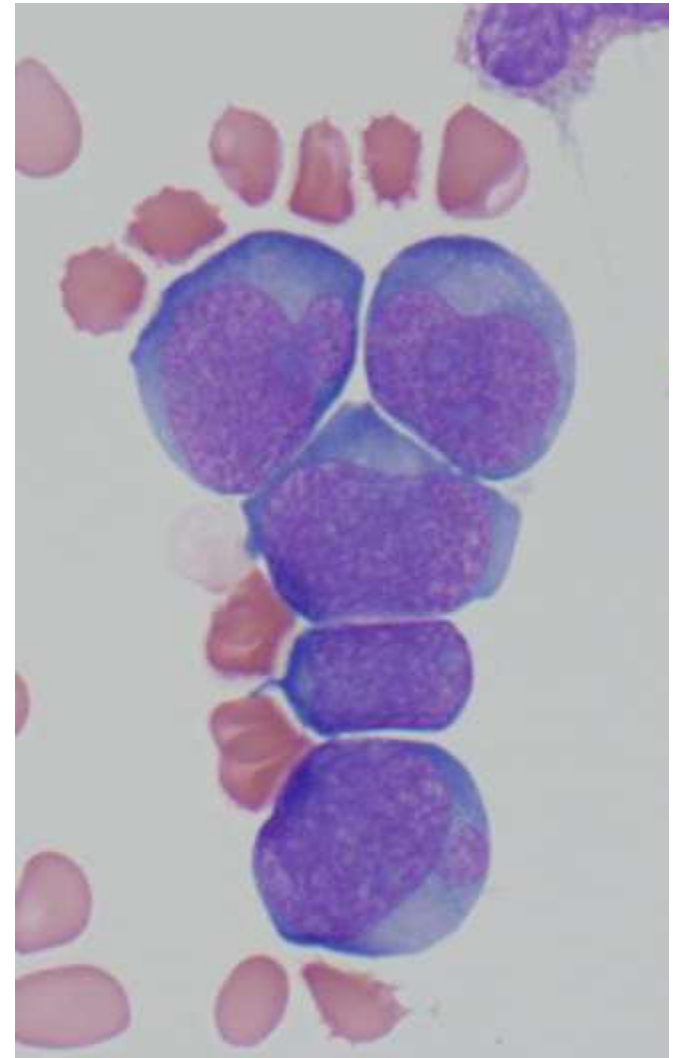


Summary

- Very large cells with immature chromatin
- CD45-, CD56+, CD117+, MPO-, CD34-

Differential diagnosis

- Leukemia
- Non-hematolymphoid tumor



Differential diagnosis of CD56+/CD45- malignancies

Table 1 Final histological diagnoses of the CD56+/CD45- malignancies

Case	Specimen	Final diagnosis
1	Lymph node	Merkel cell carcinoma
2	Parotid gland	Metastatic small cell carcinoma (unknown primary)
3	Lymph node	Metastatic small cell carcinoma (unknown primary)
4	Lymph node	Metastatic undifferentiated neuroendocrine carcinoma
5	Lymph node	Metastatic pancreatic neuroendocrine carcinoma
6	Lymph node	Merkel cell carcinoma
7	Lymph node	Metastatic undifferentiated neuroendocrine carcinoma
8	Lymph node	Merkel cell carcinoma
9	Lymph node	Metastatic small cell carcinoma (lung primary)
10	Lymph node	Metastatic small cell carcinoma (unknown primary)
11	Chest wall mass	Metastatic small cell carcinoma (unknown primary)
12	Temple mass	Neuroblastoma

Differential diagnosis of CD56+/CD45- malignancies

TABLE 2
Flow Cytometry and Immunoperoxidase Results and Final Fine-Needle Aspiration Biopsy Diagnosis

Case no.	IPOX Profile	FC	Final FNAB diagnosis
1	ND	CD45 negative CD56 positive	Small cell carcinoma
2	ND	CD71 positive CD45 negative CD56 positive	Small cell carcinoma
3	Positive-CK, CD56, NSE, chromogranin, synaptophysin Negative-desmin, CLA	CD71 positive CD45 negative CD56 positive	Small cell carcinoma
4	ND	CD71 positive CD45 negative CD56 positive	Small cell carcinoma
5	ND	CD71 positive CD45 negative CD56 positive	Small cell carcinoma
6	Positive-CK, CD56, chromogranin, NSE Negative-CLA	CD71 positive CD45 negative CD56 positive	Small cell carcinoma
7	ND	CD71 positive CD45 negative CD56 positive	Small cell carcinoma
8	ND	CD71 positive CD45 negative CD56 positive	Small cell carcinoma
9	Positive-CK Negative-CLA, NSE	CD71 positive CD45 negative CD56 positive	Merkel cell carcinoma
10	Positive-O13 Negative-CLA, desmin, chromogranin, synaptophysin	CD71 positive CD45 negative CD56 positive	Ewing sarcoma/PNET

IPOX: immunoperoxidase; FC: flow cytometry; FNAB: fine-needle aspiration biopsy; ND not done; CK: cytokeratins; NSE: neuron-specific enolase; CLA: common leukocyte antigen; PNET: primitive neuroectodermal tumor.

Additional history

- Metastatic Merkel cell carcinoma

Merkel cell carcinoma

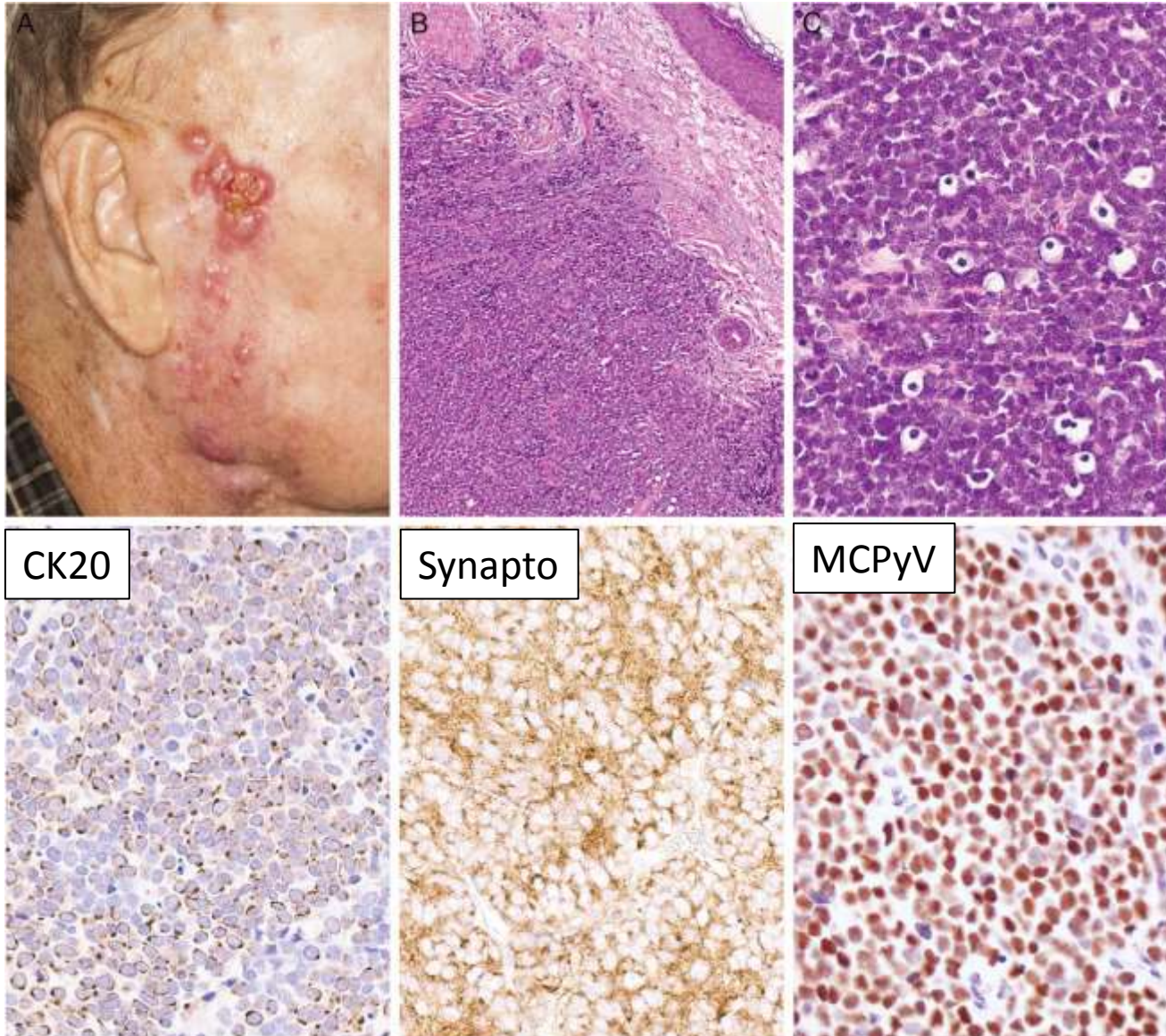
Clinical features:

- Typically arises as a painless, rapidly growing, single red or purple cutaneous nodule in the head, neck or the extremities.
- Up to 30% of the patients have metastatic disease at presentation
- Clinical course is often aggressive with a high risk for tumor recurrence

Putative cell of origin:

- Merkel cells found near the nerve terminals that are thought to be mechanoreceptors

Representative clinical picture showing clusters of tumour papules and nodules in the right cheek of a patient with Merkel cell carcinoma (MCC).



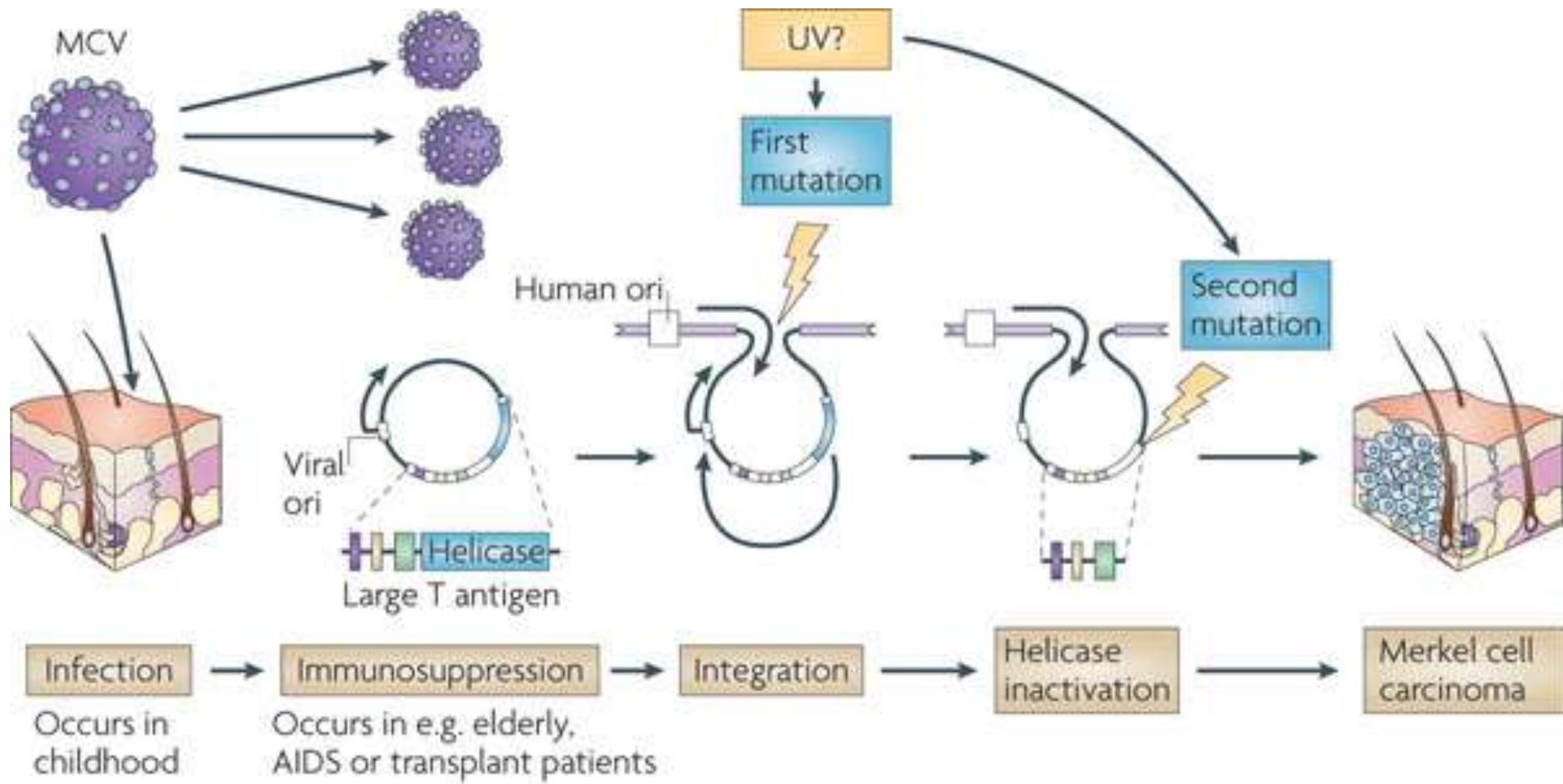
Merkel cell carcinoma Immunohistochemistry

Positive Stains	Negative Stains
AE1/AE3 (100%)	TTF-1
CAM 5.2 (100%)	Leukocyte common antigen
CK20 (93%)	CD20
CD56 (100%)	CD3
Bcl-2 (100%)	CD34
Neuron specific enolase (NSE) (100%)	
Synaptophysin (87%)	
Chromogranin-A (73%)	
TdT (53%)	
CD117 (53%)	

Merkel cell carcinoma (MCC)

Biology

- ~80% of MCCs are associated with Merkel cell polyomavirus (MCPyV)
- ~80% of North American blood donors older than 50 have been exposed to MCPyV
- Risk factors for MCC include UV exposure, immunosuppression, and arsenic exposure



Nature Reviews | Cancer

Summary

- Utility of CD56-positive/CD45-negative immunophenotype in the identification of neuroendocrine malignancies
 - Small cell carcinomas, Merkel cell carcinomas, metastatic undifferentiated neuroendocrine carcinomas, metastatic pancreatic neuroendocrine carcinoma, neuroblastoma

Patient follow up

- Dec-Jan: 3 cycles of carboplatin + etoposide
- February: Switched to CAV
(cyclophosphamide, adriamycin/doxorubicin, vincristine)

References

1. Bryson GJ, Lear D, Williamson R, et al. Detection of the CD56+/CD45–immunophenotype by flow cytometry in neuroendocrine malignancies. *J Clin Pathol* 2002; 55: 535.
2. Farinola MA, Weir EG, Ali SZ. CD56 expression of neuroendocrine neoplasms on immunophenotyping by flow cytometry. *Cancer(Cancer Cytopathol)* 2003;99:240–246.
3. Shield PW, Crous H. Fine-needle aspiration cytology of Merkel cell carcinoma-a review of 69 cases. *Diagn Cytopathol*. 2014 Nov;42(11):924-8.
4. Mauzo SH, Ferrarotto R, Bell D, Torres-Cabala CA, Tetzlaff MT, Prieto VG, Aung PP. Molecular characteristics and potential therapeutic targets in Merkel cell carcinoma. *J Clin Pathol*. 2016 Jan 27. pii: jclinpath-2015-203467. doi: 10.1136/jclinpath-2015-203467. [Epub ahead of print]
5. Moore PS, and Chang Y. Why do viruses cause cancer? Highlights of the first century of human tumour virology. *Nat Rev Cancer* 2010; 10: pp. 878-889

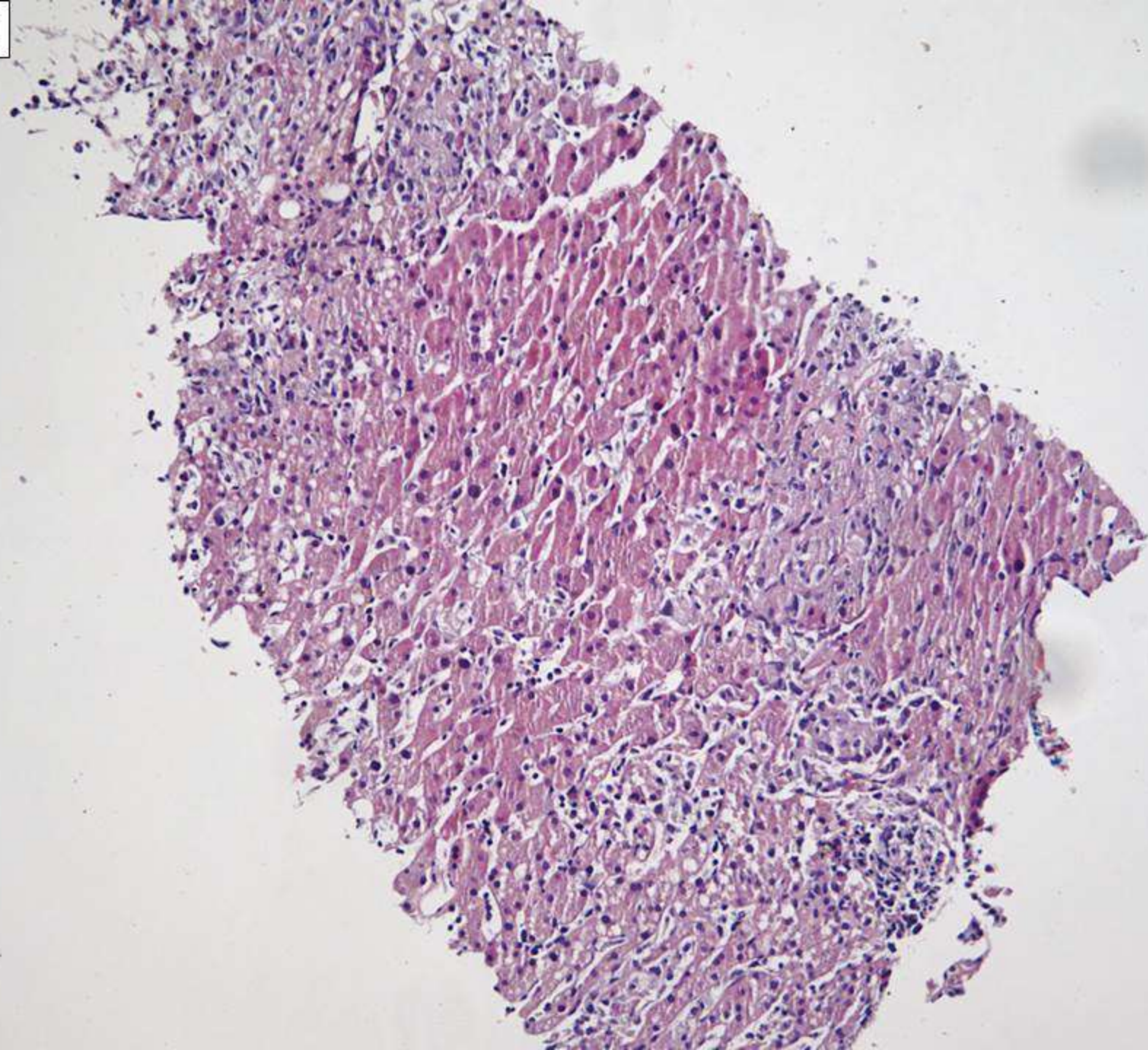
SB 6049

Sebastian Fernandez-Pol/Dita Gratzinger; Stanford

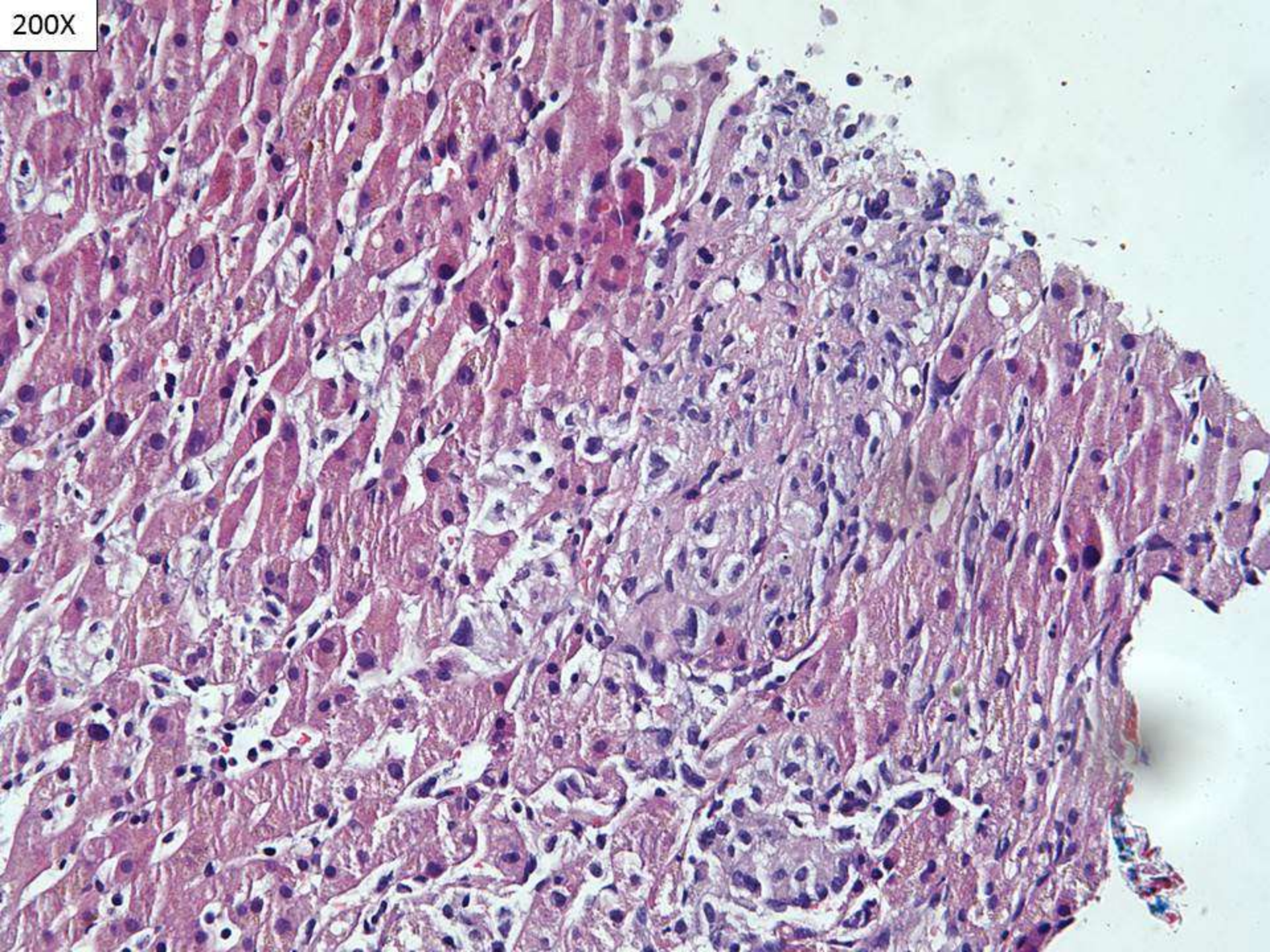
77-year-old female with multiple liver lesions.

(case courtesy of Bijayee Shrestha; El Camino Hospital)

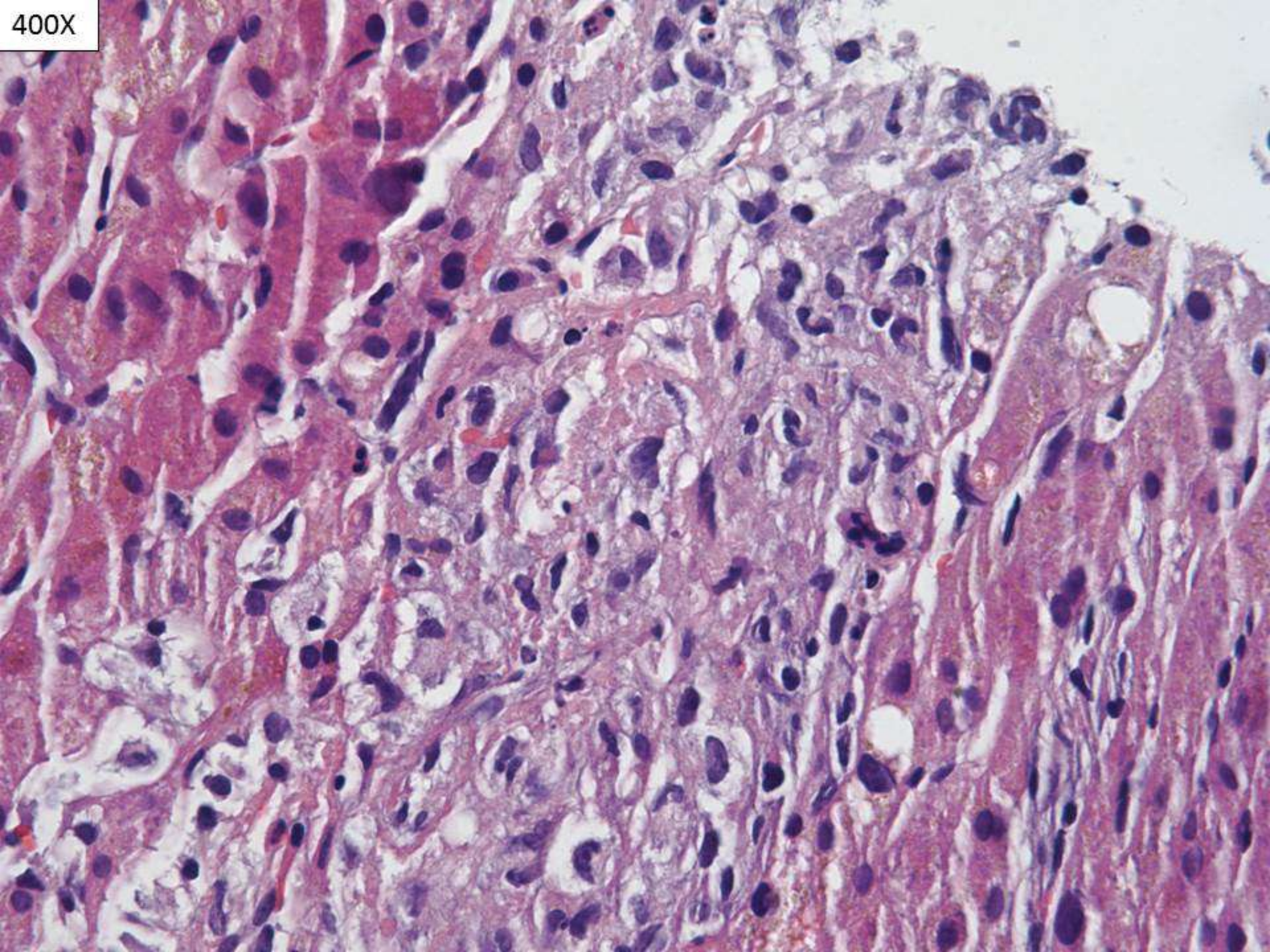
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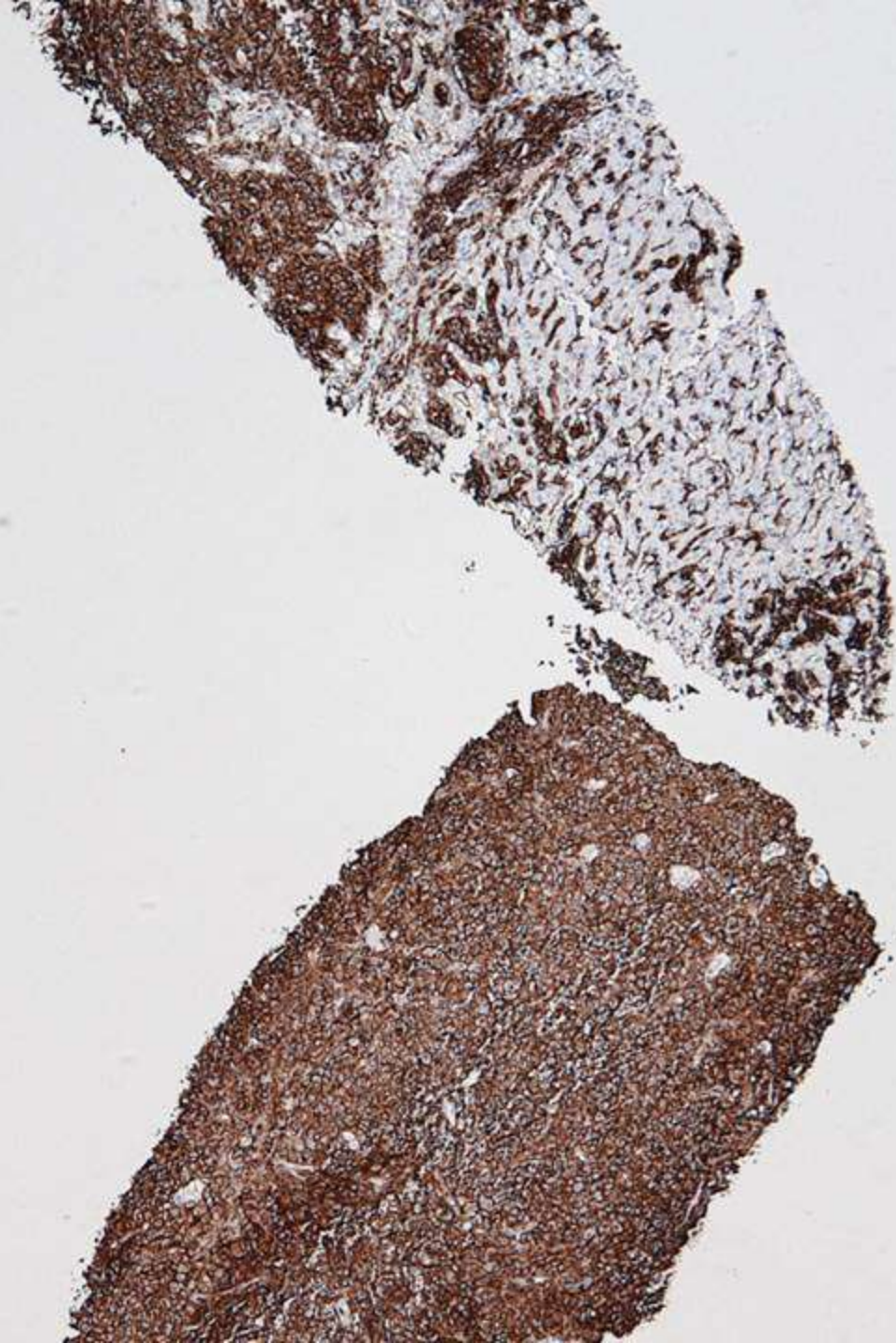
200X



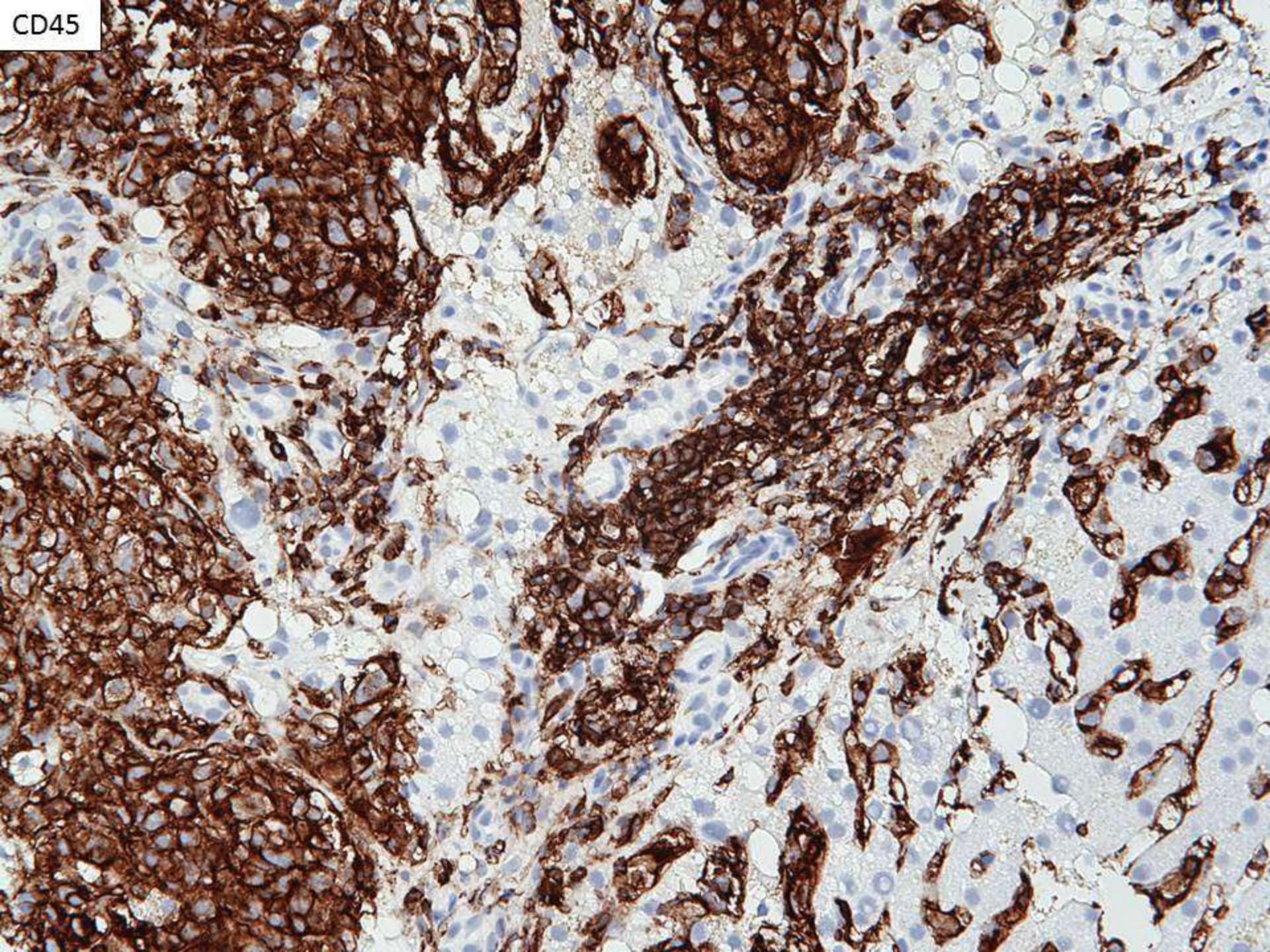
400X



CD45



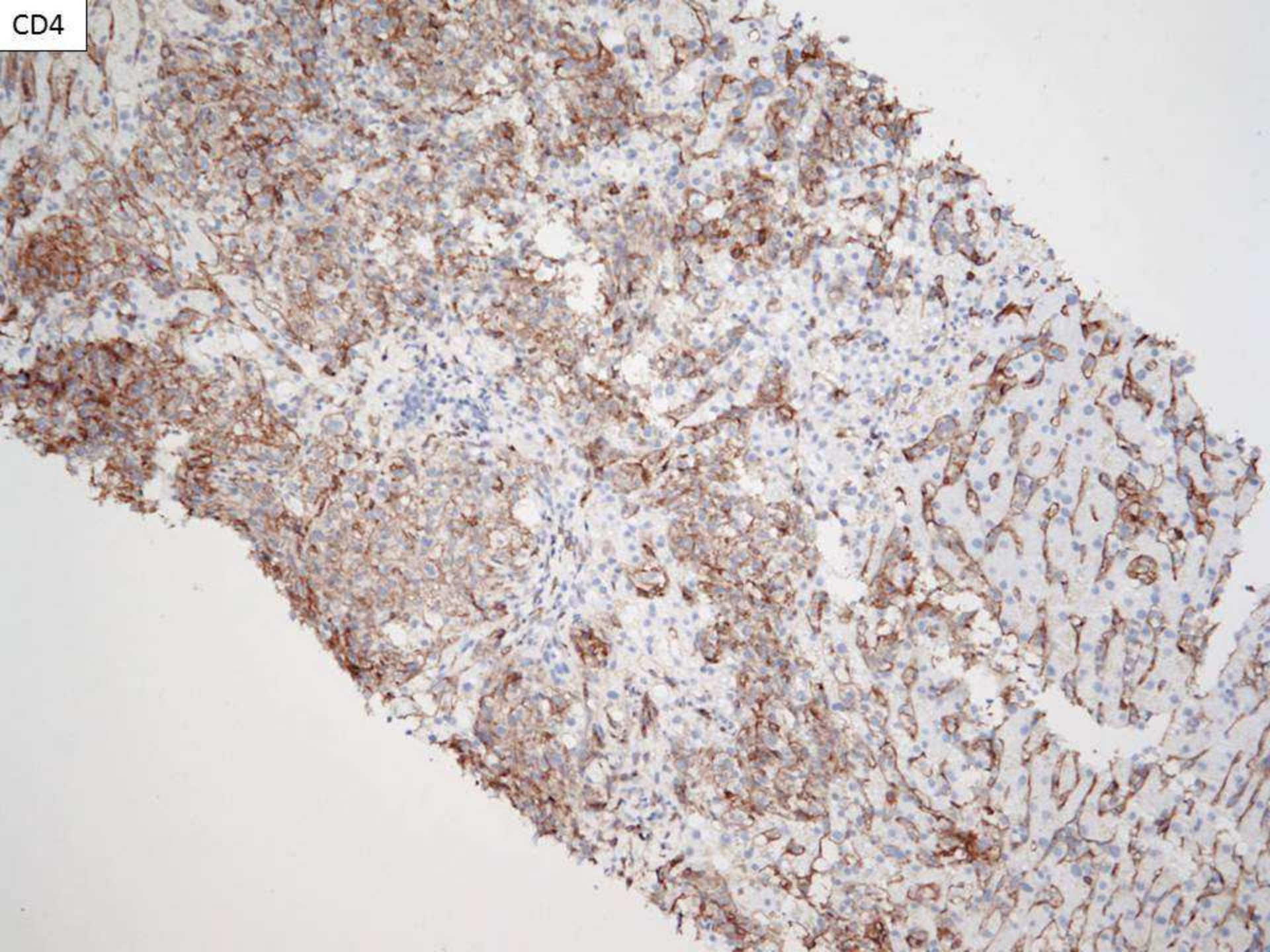
CD45



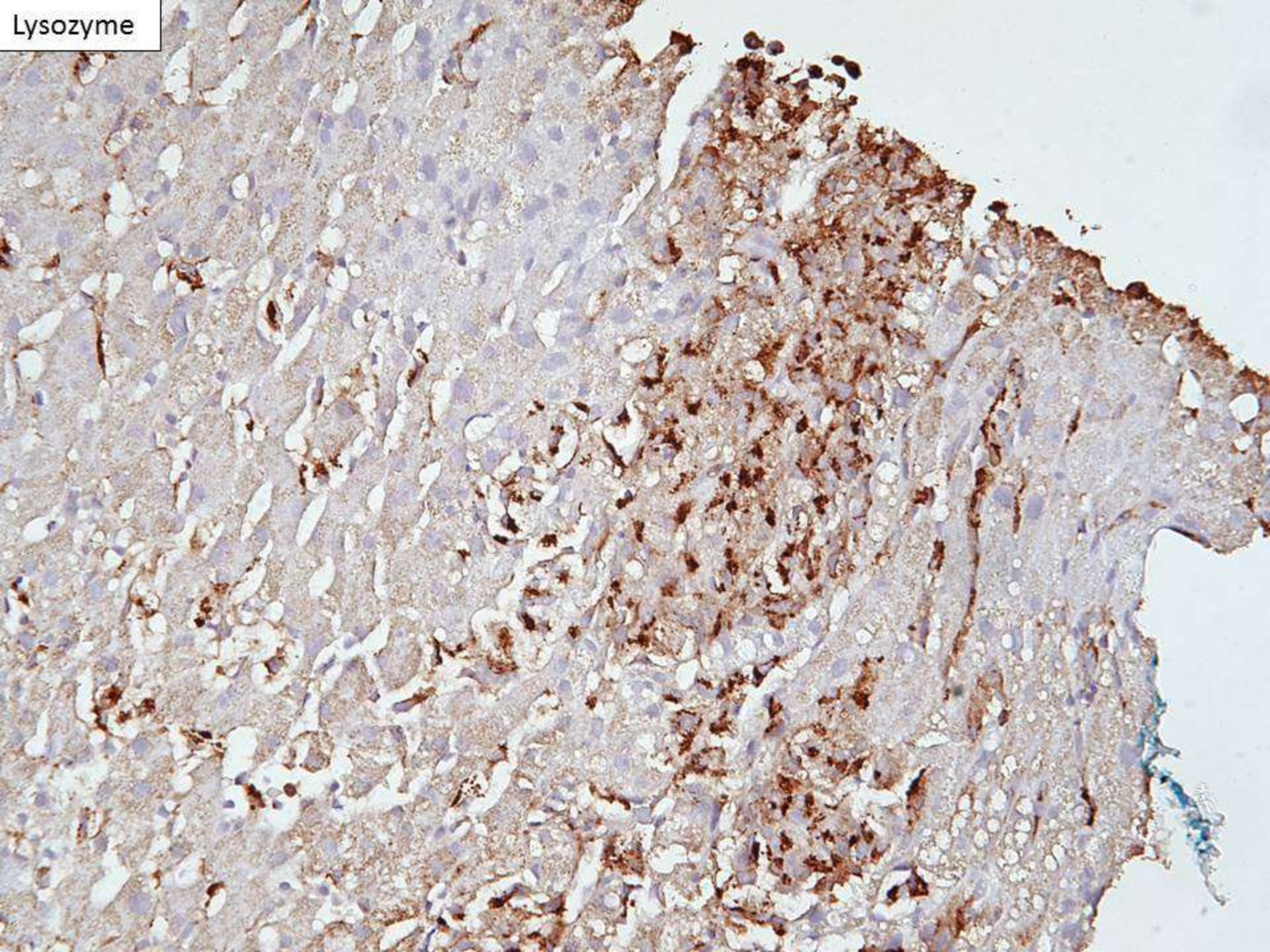
CD43



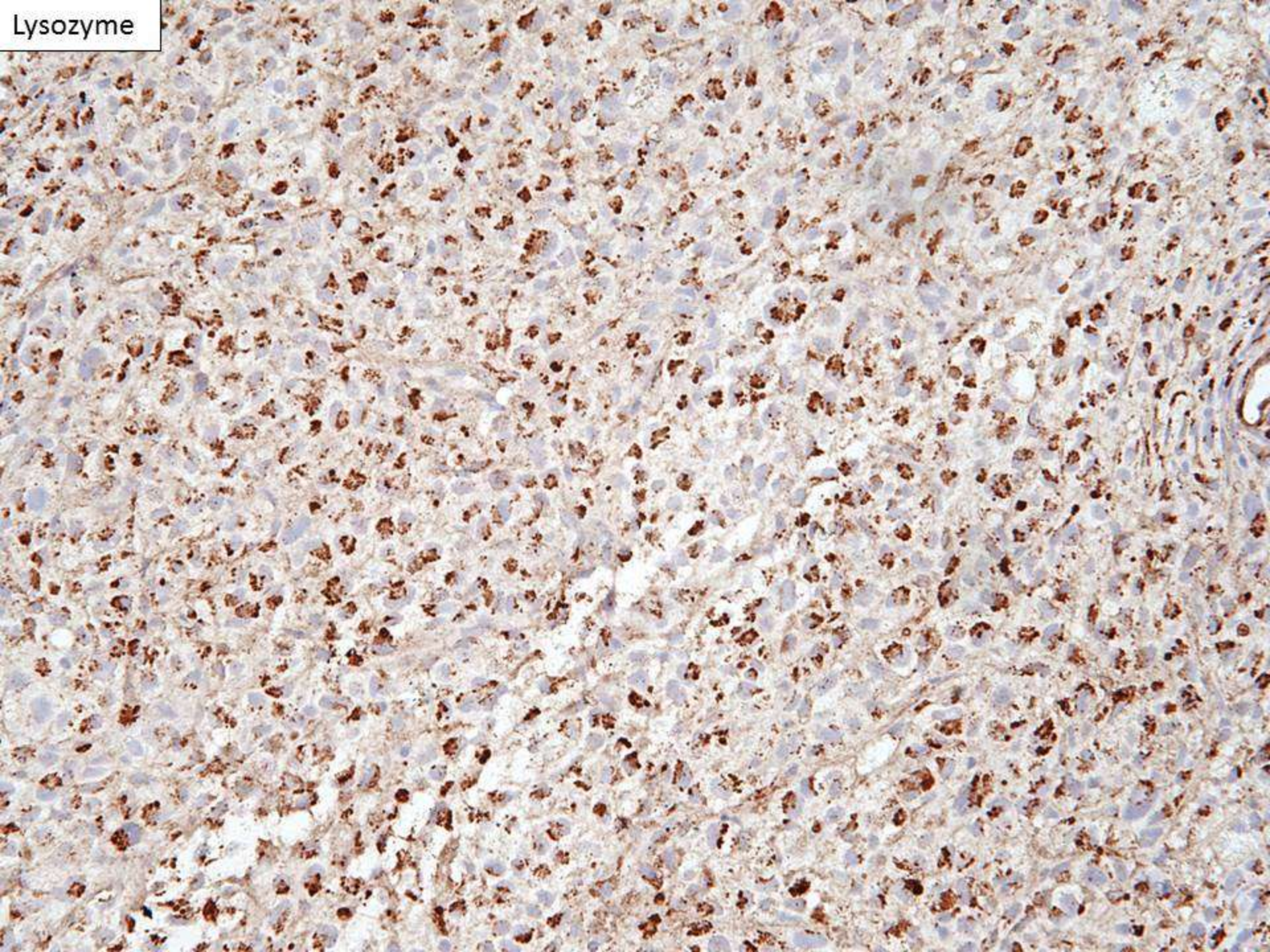
CD4



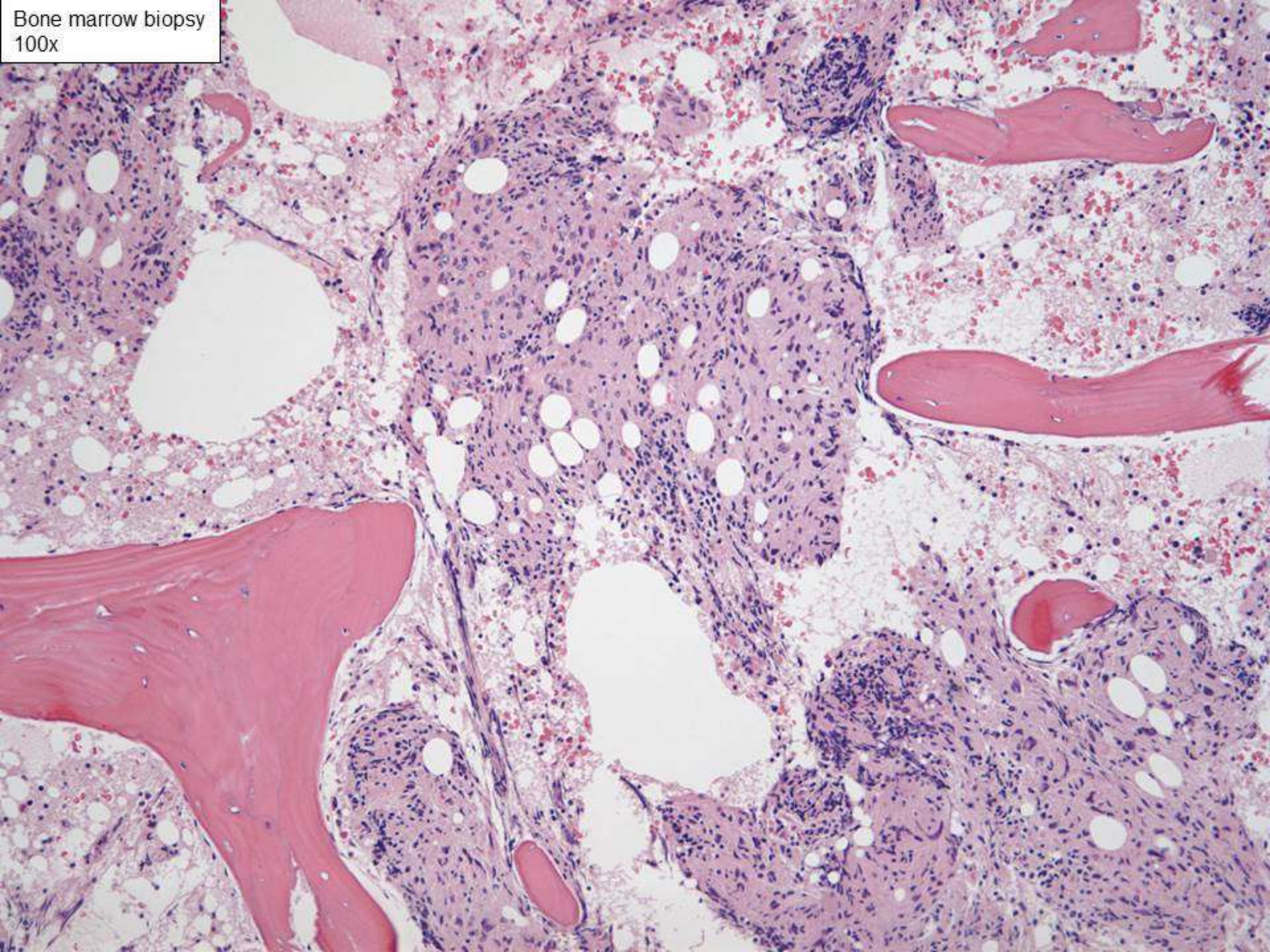
Lysozyme



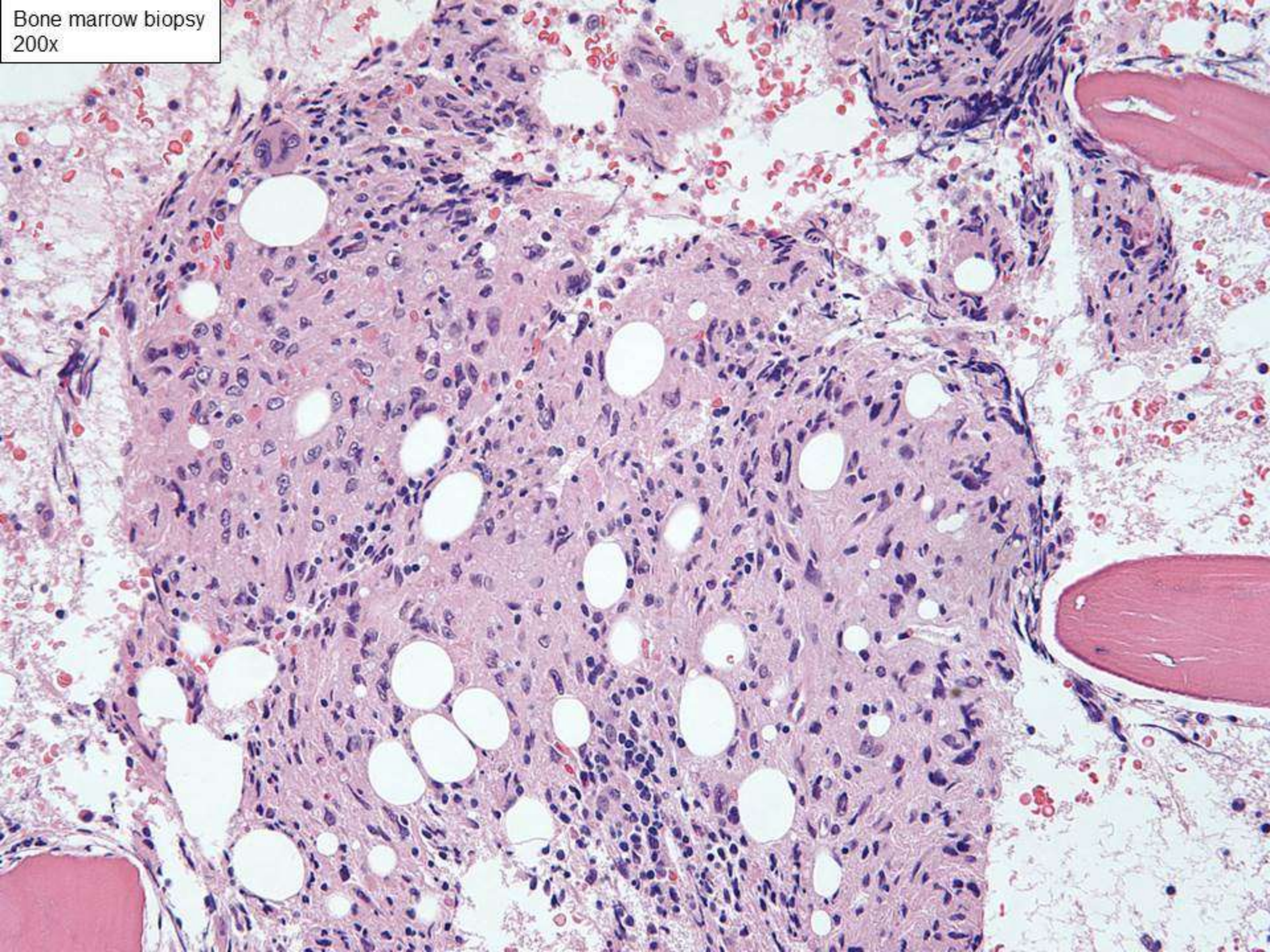
Lysozyme



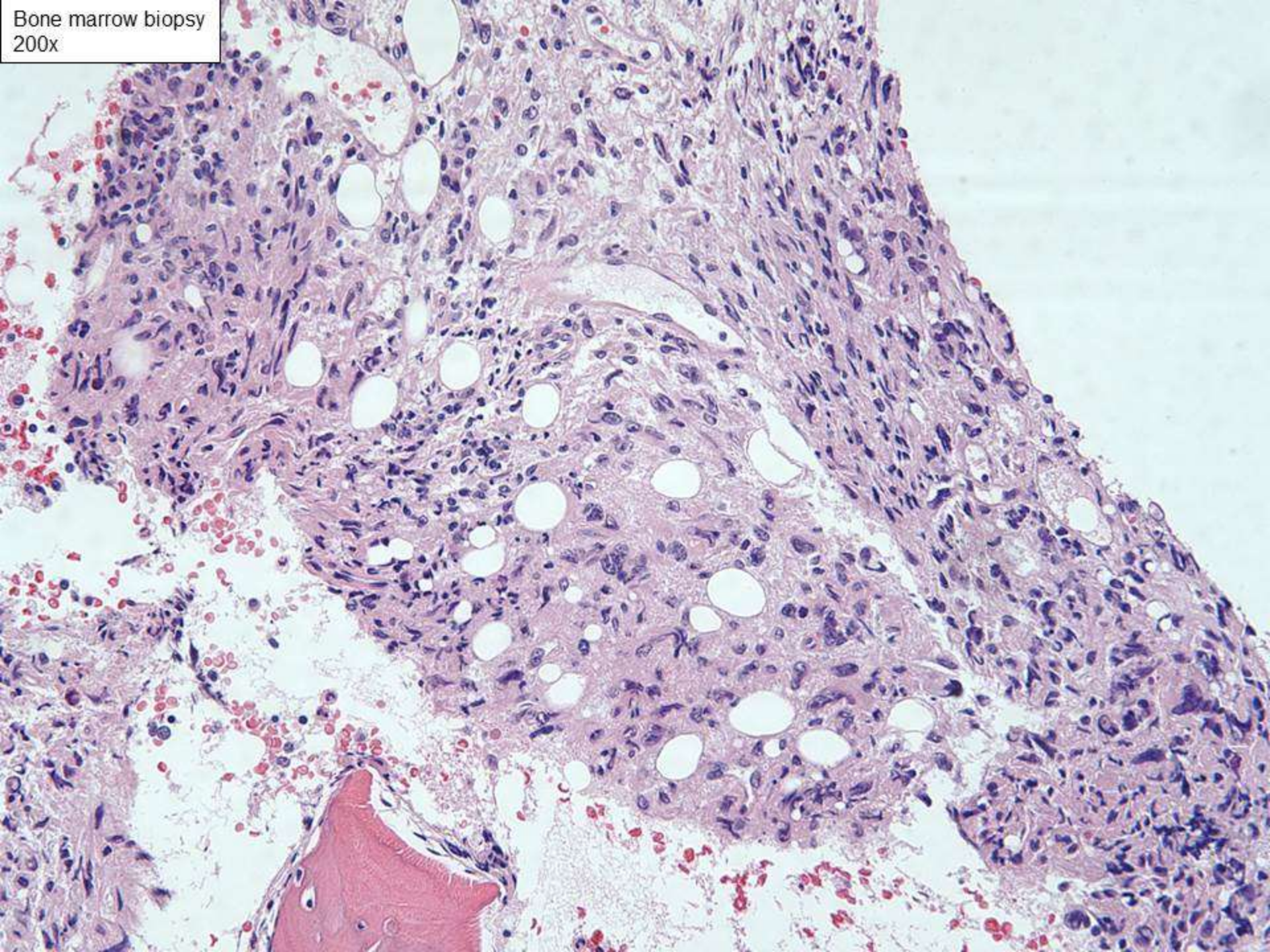
Bone marrow biopsy
100x



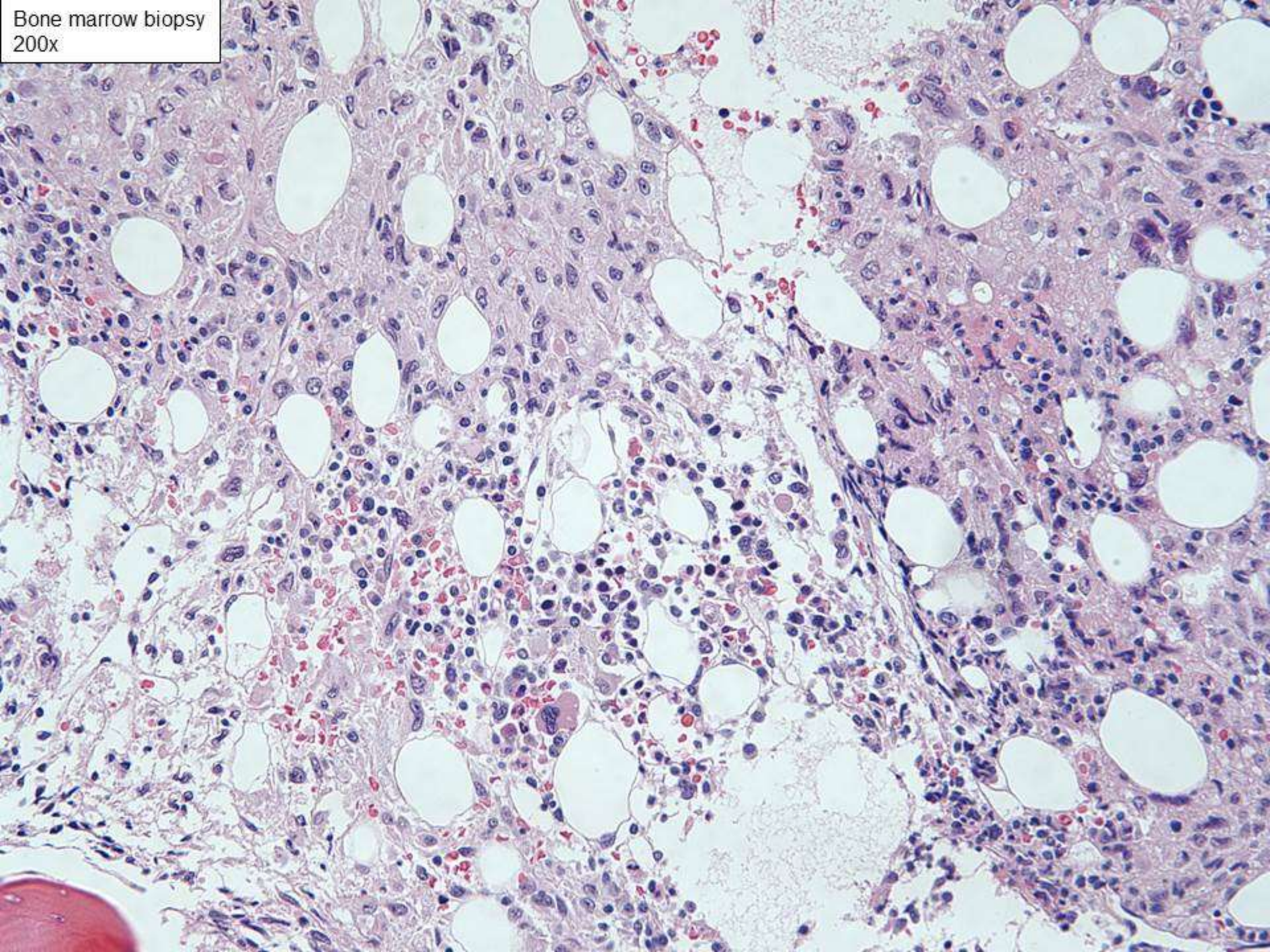
Bone marrow biopsy
200x



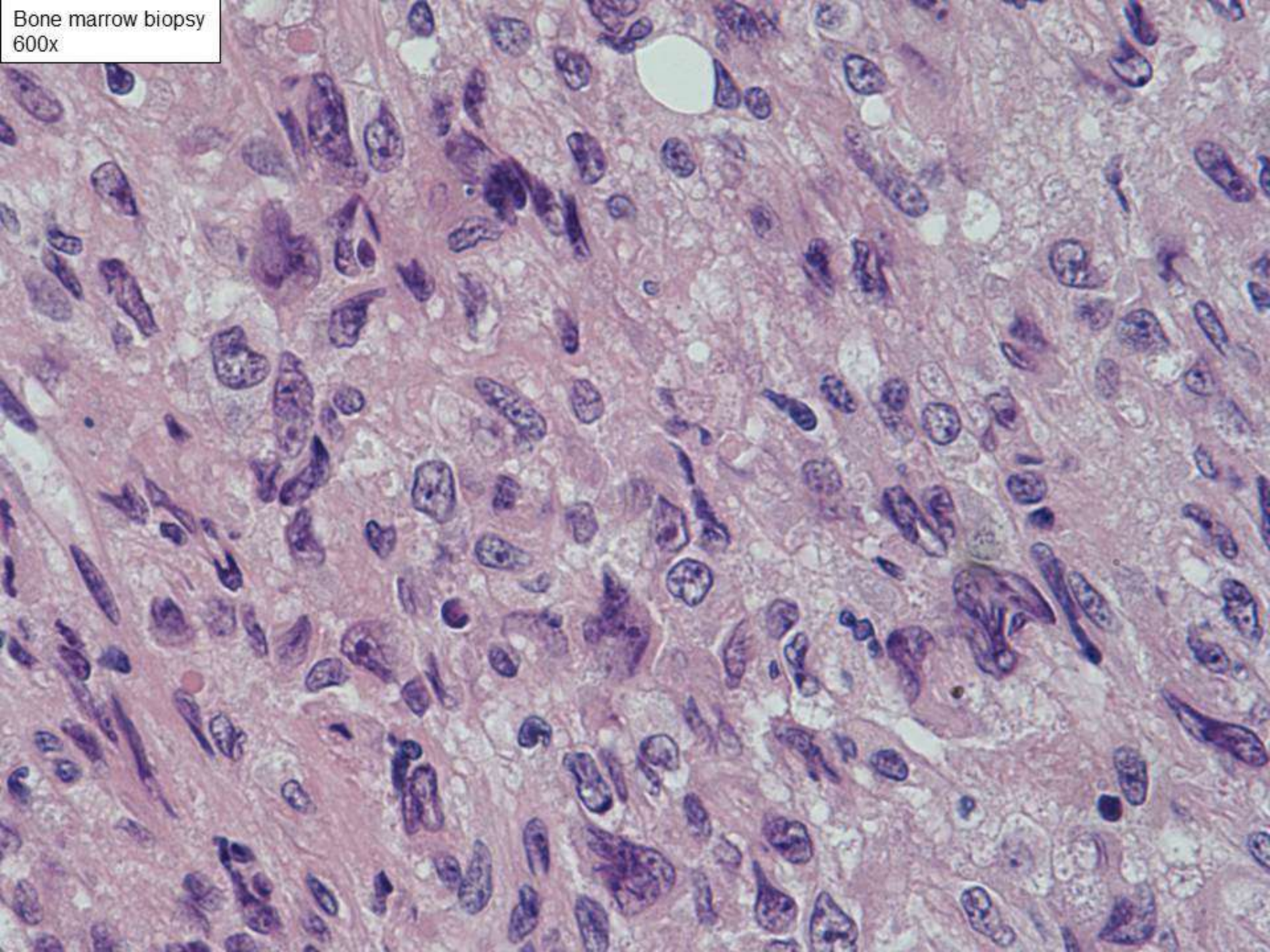
Bone marrow biopsy
200x



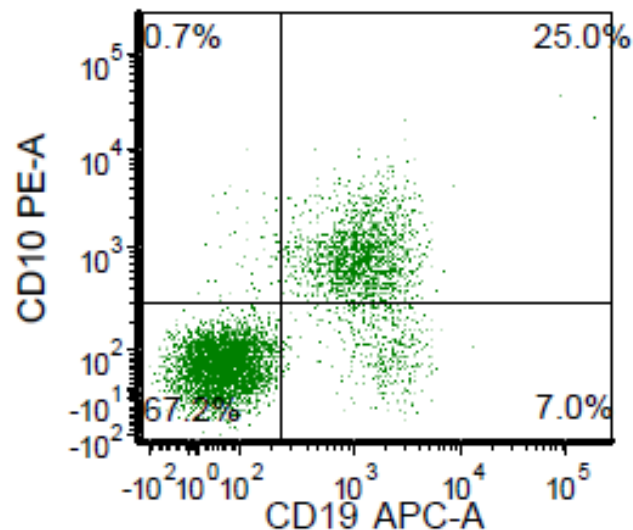
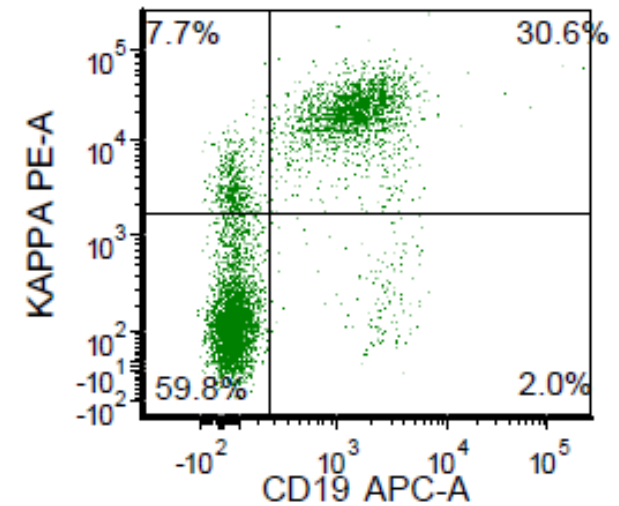
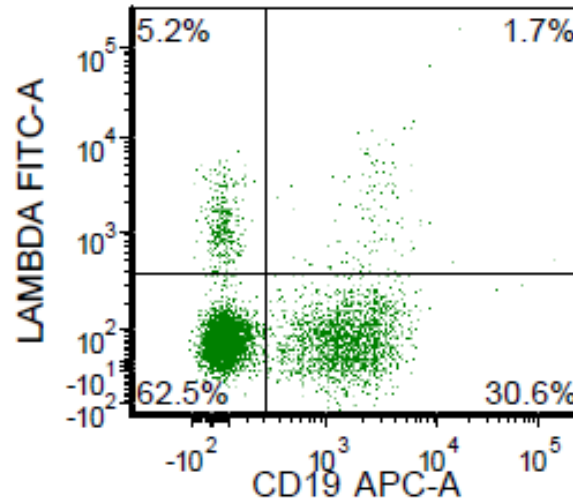
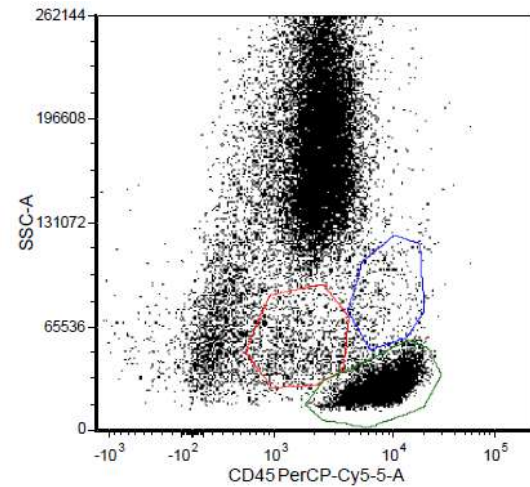
Bone marrow biopsy
200x



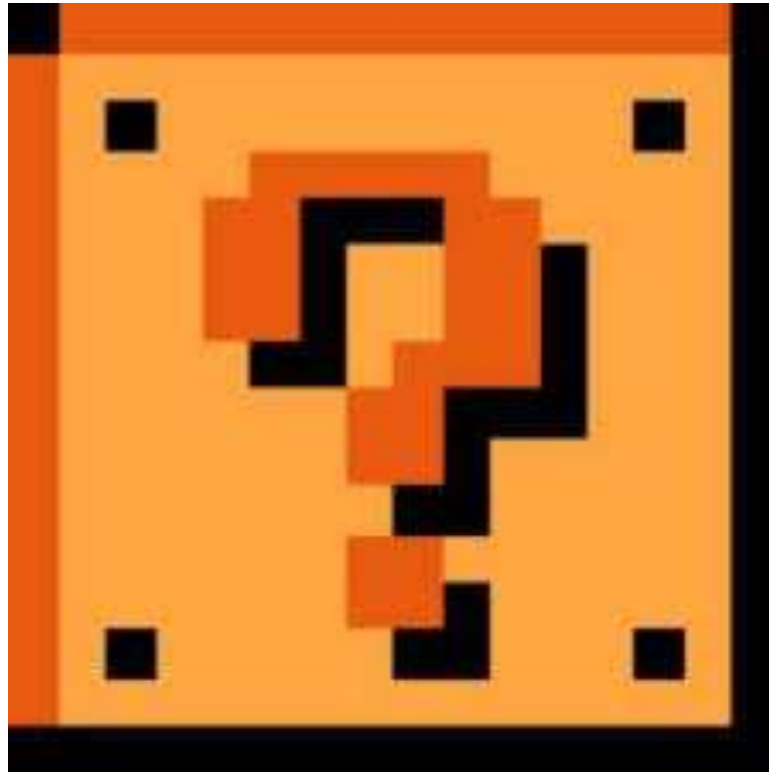
Bone marrow biopsy
600x



Bone marrow biopsy flow cytometry



DIAGNOSIS?



Differential diagnosis

- Myeloid sarcoma (with monocytic differentiation)
- Histiocytic sarcoma

Myeloid sarcoma immunophenotype

Pileri et al, 2007

- 92 cases:
 - CD68/KP1 (100%)
 - MPO (83.6%)**
 - CD117 (80.4%)**
 - CD99 (54.3%)
 - CD68/PG-M1 (51%)
 - CD34 (43.4%)**
 - TdT (31.5%)**

Our Case

Stain	Result
CD43	Positive (dim)
CD68	Positive (dim)
Lysozyme	Positive (liver) Negative (BM)
CD4	Positive (dim)
CD56	Partial variable
BCL6	Positive
CD34	Negative
CD117	Negative
TdT	Negative
MPO	Negative

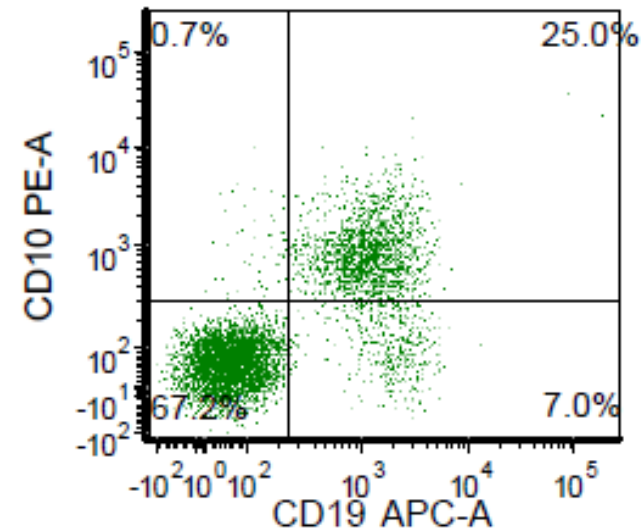
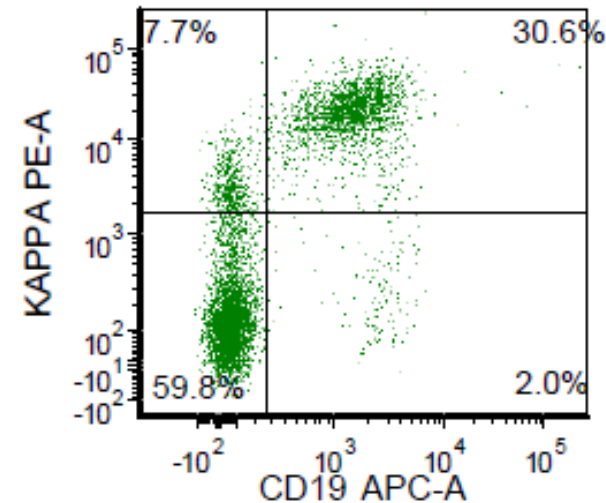
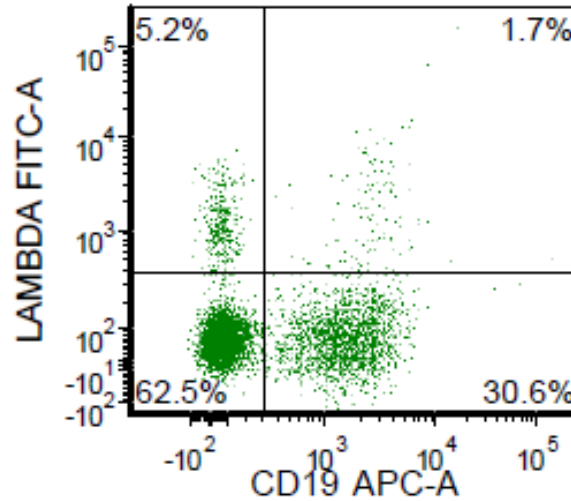
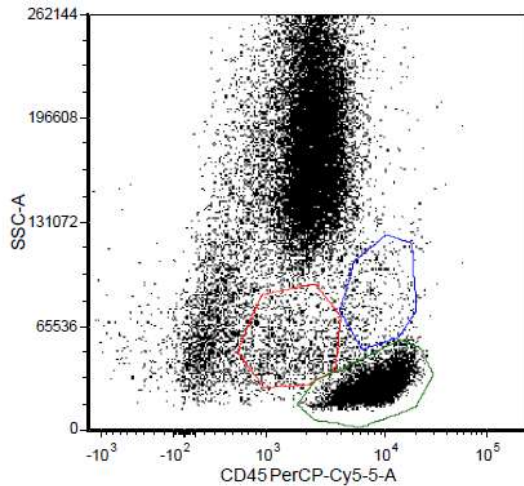
Histiocytic sarcoma immunophenotype

- No great specific markers
- Positive for: CD45, CD68, CD163, lysozyme
- Must rule out other entities

Our Case

Stain	Result
CD43	Positive (dim)
CD68	Positive (dim)
Lysozyme	Positive (liver) Negative (BM)
CD4	Positive (dim)
CD56	Partial variable
BCL6	Positive
CD34	Negative
CD117	Negative
TdT	Negative
MPO	Negative

Bone marrow biopsy flow cytometry



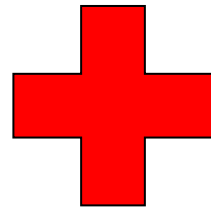
CD10 POSITIVE, KAPPA MONOTYPIC B CELL POPULATION



Follicular lymphoma

Summary so far

Histiocytic sarcoma OR myeloid sarcoma with monocytic differentiation



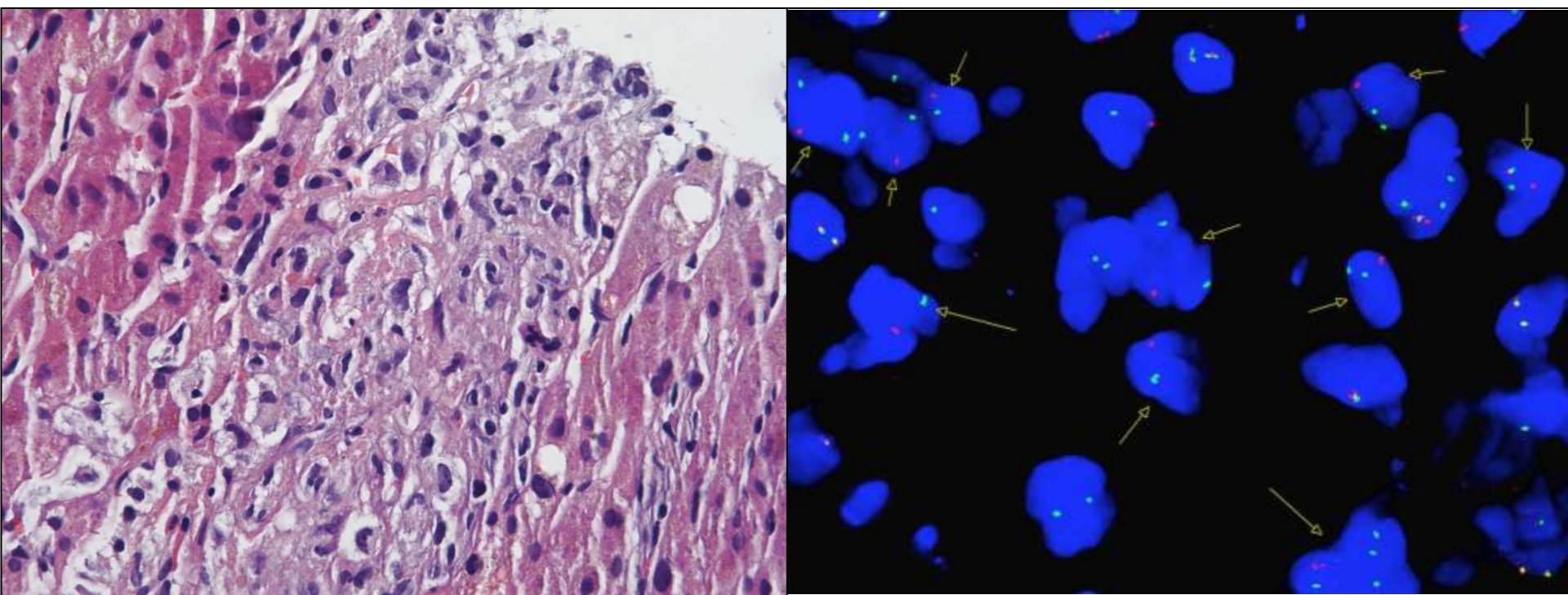
Follicular lymphoma



Does this combination suggest anything?

Malignancies associated with histiocytic sarcoma	Clonal relationship	References
Follicular lymphoma	t(14;18), Identical clonal <i>IGH/BCL2</i> rearrangements Comparative genome hybridization	Feldman et al, Blood, 2008 Zhang et al, Int J Hematol, 2009 Brunner et al, Leukemia, 2014
AML		Zhao et al, 2015
Hairy cell leukemia	BRAFV600E and CGH	Michonneau et al, J Clin Oncol, 2014
Mantle cell lymphoma	CCND1-IGH IGH rearrangements	Hure et al, J Clin Oncol, 2012
MALT type lymphoma		Alvaro et al, Am J Surg Pathol, 1996
DLBCL	IGH/BCL2 fusion gene	Wang et al, Am J Surg Pathol, 2011
ALL	Clonal IgH and TCRγ gene rearrangements	Feldman et al, Lancet Oncol, 2004 McClure et al, Leuk Res, 2010 Castro et al, Pediatric Dev Pathol, 2010 Kumar et al, Pediatr Blood Cancer, 2011 Bouabdallah et al, Br J Haematol, 2001
CLL/SLL	Identical clonal <i>IGH</i> gene rearrangements	Shao et al, Mod Pathol, 2011
CMML	Karyotype evidence	Mori et al, Int J Hematol, 2010
Mediastinal germ cell tumors		Song, Int J Surg Pathol, 2005
Idiopathic myelofibrosis		Fukunaga et al, Arch Pathol Lab Med. 2004
CML	BCR-ABL	Ansari et al, Eur J Haematol, 2016

FISH on the liver biopsy showing separation of 5' and 3' BCL2 probes



Final diagnosis

- **Liver biopsy**
 - Histiocytic sarcoma with BCL2 gene rearrangement by FISH
- **Bone marrow, aspirate and biopsy**
 - Histiocytic sarcoma
 - Follicular lymphoma, grade 1-2
- **Bone marrow, aspirate, flow cytometry immunophenotyping**
 - CD10 positive, kappa-monotypic B-cell population
- **Bone marrow, aspirate, cytogenetic interpretation**
 - Normal 46,XX female karyotype
 - FISH positive for BCL2 gene rearrangement, consistent with follicular lymphoma

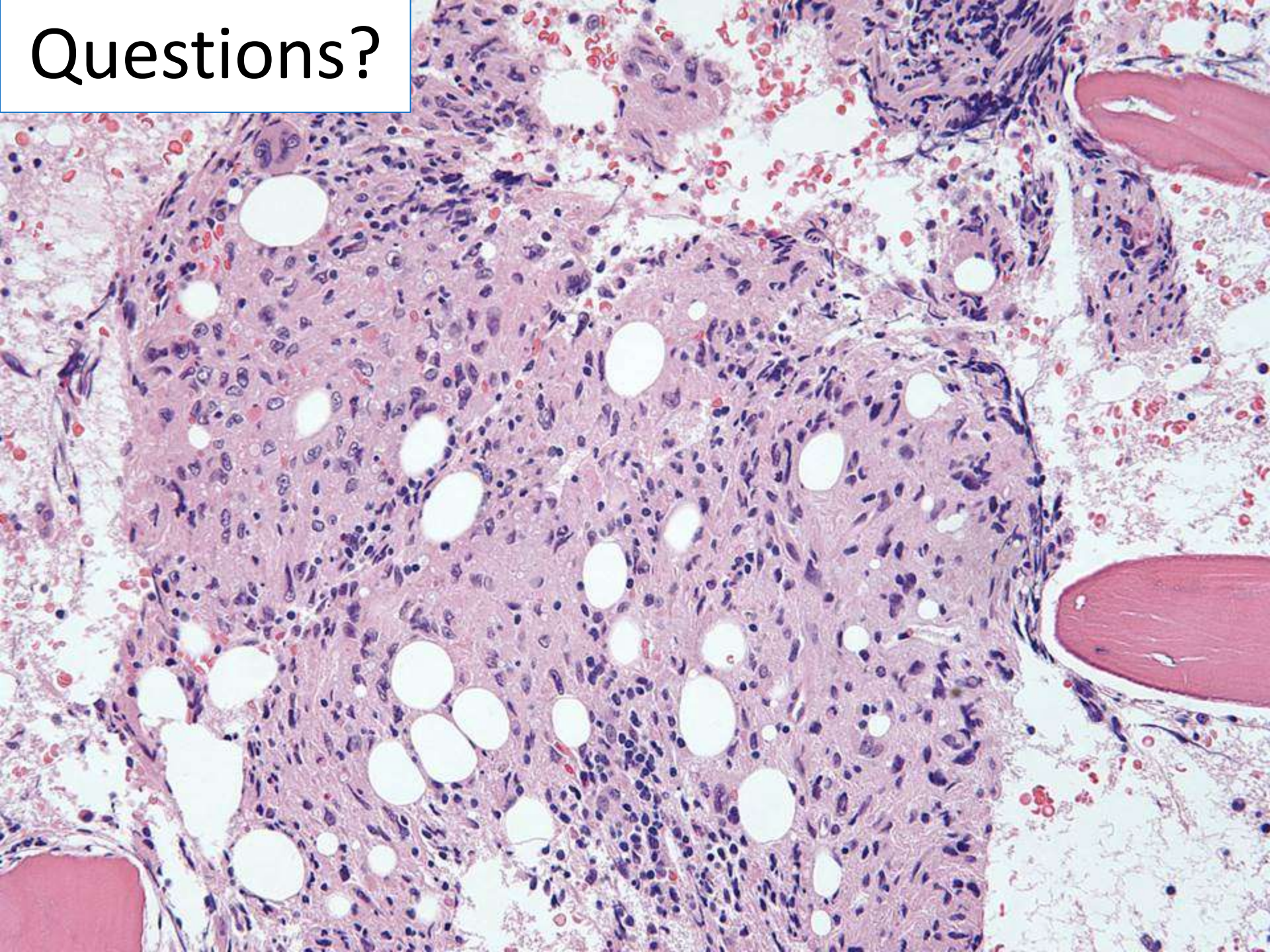
Histiocytic sarcoma summary

- Histology:
 - Malignancy with morphologic and immunophenotypic features that resemble those of mature tissue histiocytes
 - Must rule out mimics:
 - Carcinoma
 - Melanoma
 - Anaplastic large cell lymphoma
 - Diffuse large B-cell lymphoma
 - Myeloid sarcoma
 - Undifferentiated pleomorphic sarcoma (MFH)
- If HS is in the differential diagnosis, look for another malignancy
- Molecular:
 - t(14;18) rearrangements may help to distinguish histiocytic sarcoma from myeloid sarcoma

References

1. Feldman A. L., Arber D. A., Pittaluga S., et al. Clonally related follicular lymphomas and histiocytic/dendritic cell sarcomas: evidence for transdifferentiation of the follicular lymphoma clone. *Blood*.2008;111(12):5433–5439.
2. Chao MP, Seita J, Weissman IL. Establishment of a normal hematopoietic and leukemia stem cell hierarchy. *Cold Spring Harb Symp Quant Biol*. 2008;73:439–449.
3. Wilson CS, Medeiros LJ. Extramedullary Manifestations of Myeloid Neoplasms. *Am J Clin Pathol*. 2015 Aug;144(2):219-39.
4. Pileri SA, Ascani S, Cox MC, et al. Myeloid sarcoma: clinico-pathologic, phenotypic and cytogenetic analysis of 92 adult patients. *Leukemia*. 2007;21:340–350.
5. Pileri SA, Grogan TM, Harris NL, Banks P, Campo E, Chan JK. et al. Tumours of histiocytes and accessory dendritic cells: an immunohistochemical approach to classification from the International Lymphoma Study Group based on 61 cases. *Histopathology*. 2002;41(1):1–29.
6. Hornick JL, Jaffe ES, Fletcher CD. Extranodal histiocytic sarcoma: clinicopathologic analysis of 14 cases of a rare epithelioid malignancy. *Am J Surg Pathol*. 2004;28:1133–44.
7. Brunner P et al. Follicular lymphoma transformation into histiocytic sarcoma: indications for a common neoplastic progenitor. *Leukemia*. 2014 Sep;28(9):1937-40.

Questions?

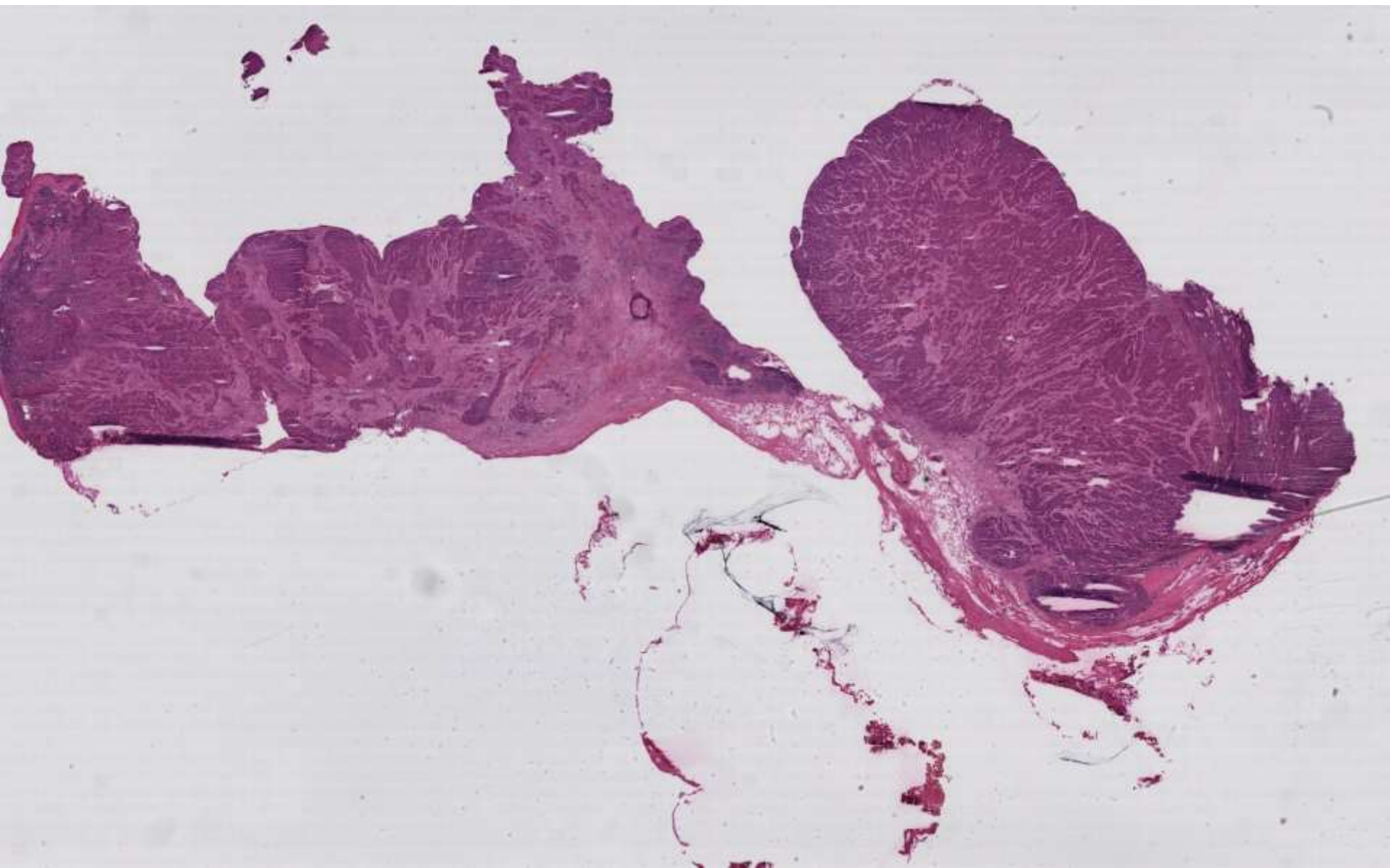


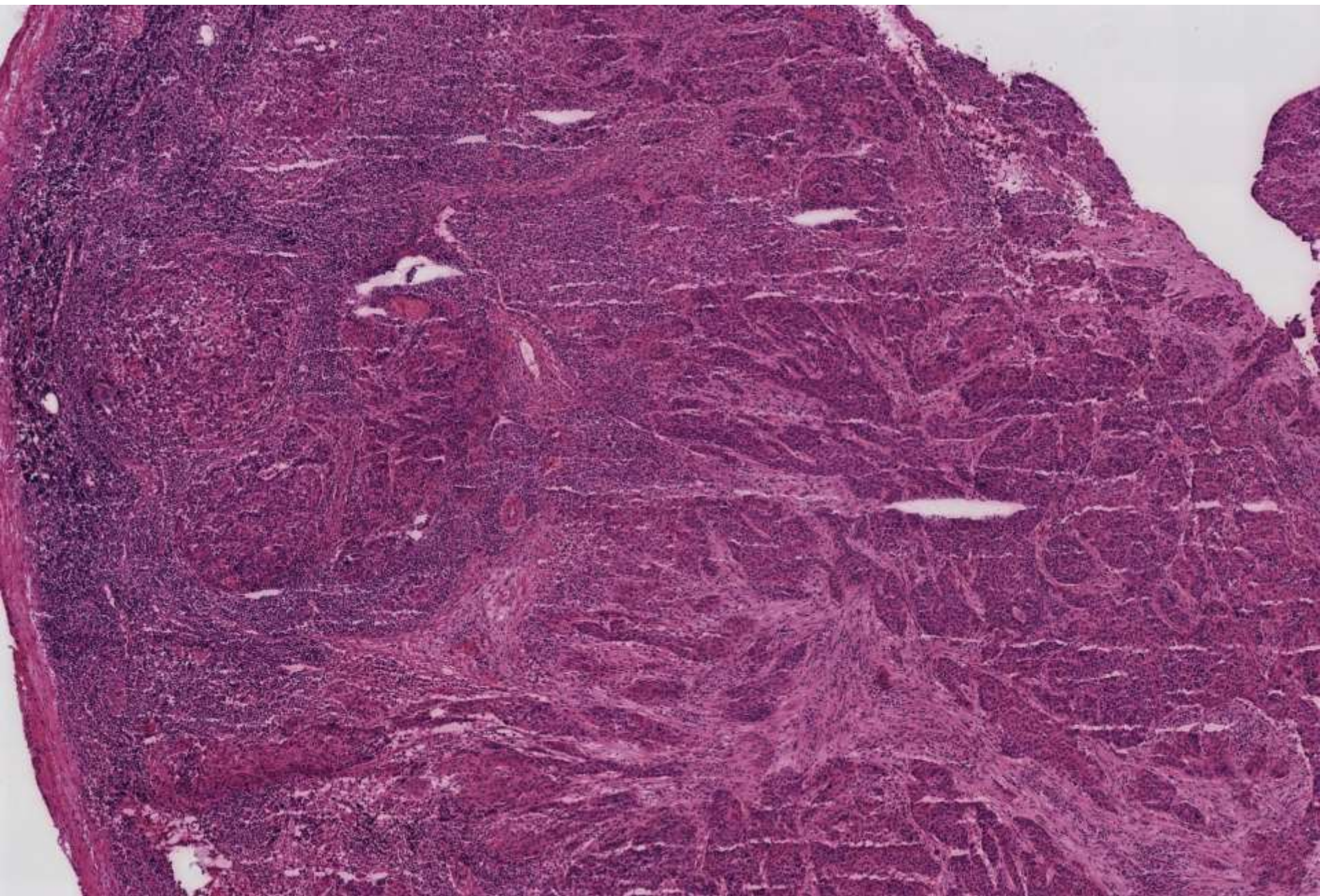
SB 6050

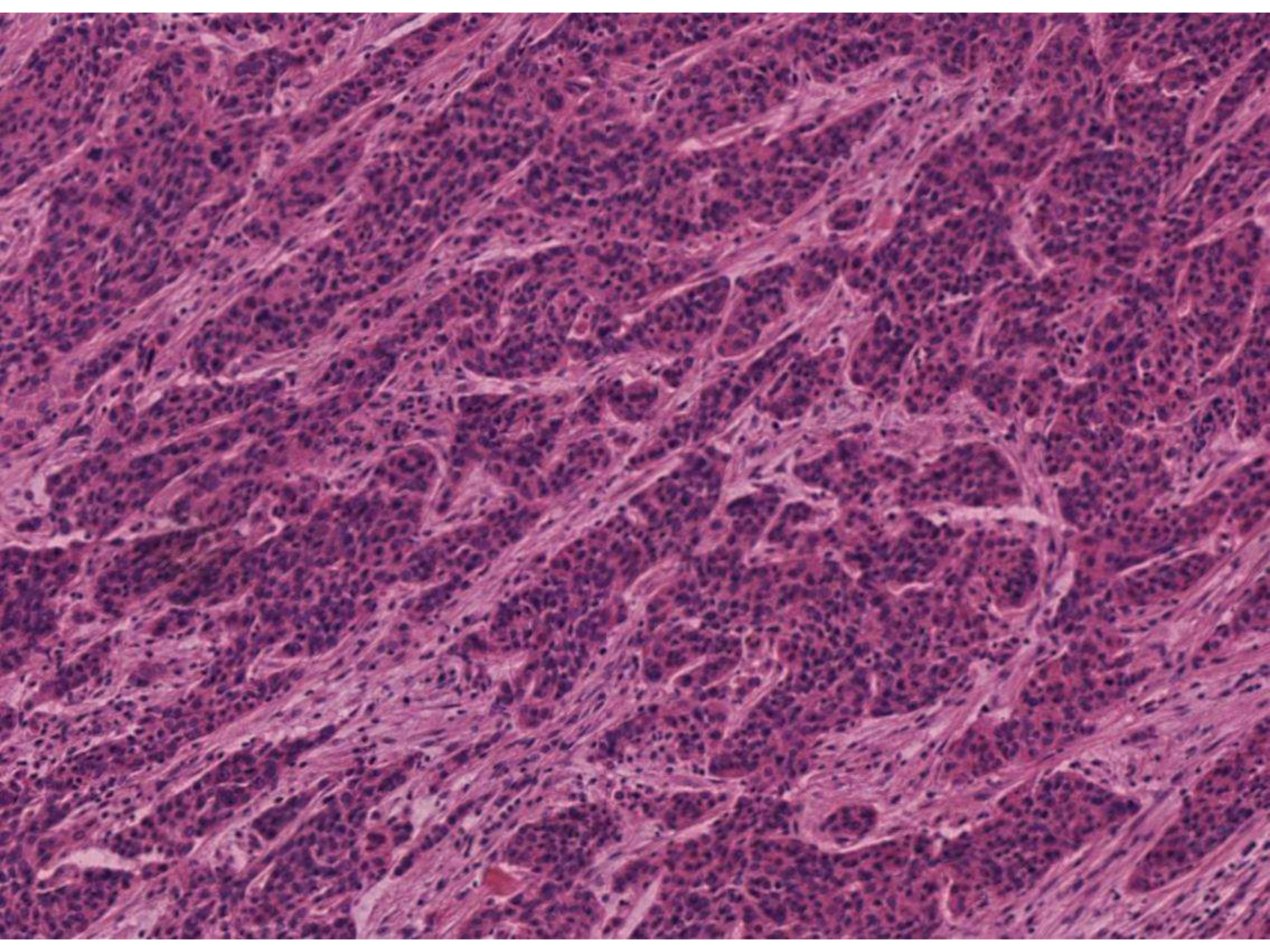
Ankur Sangoi; El Camino Hospital

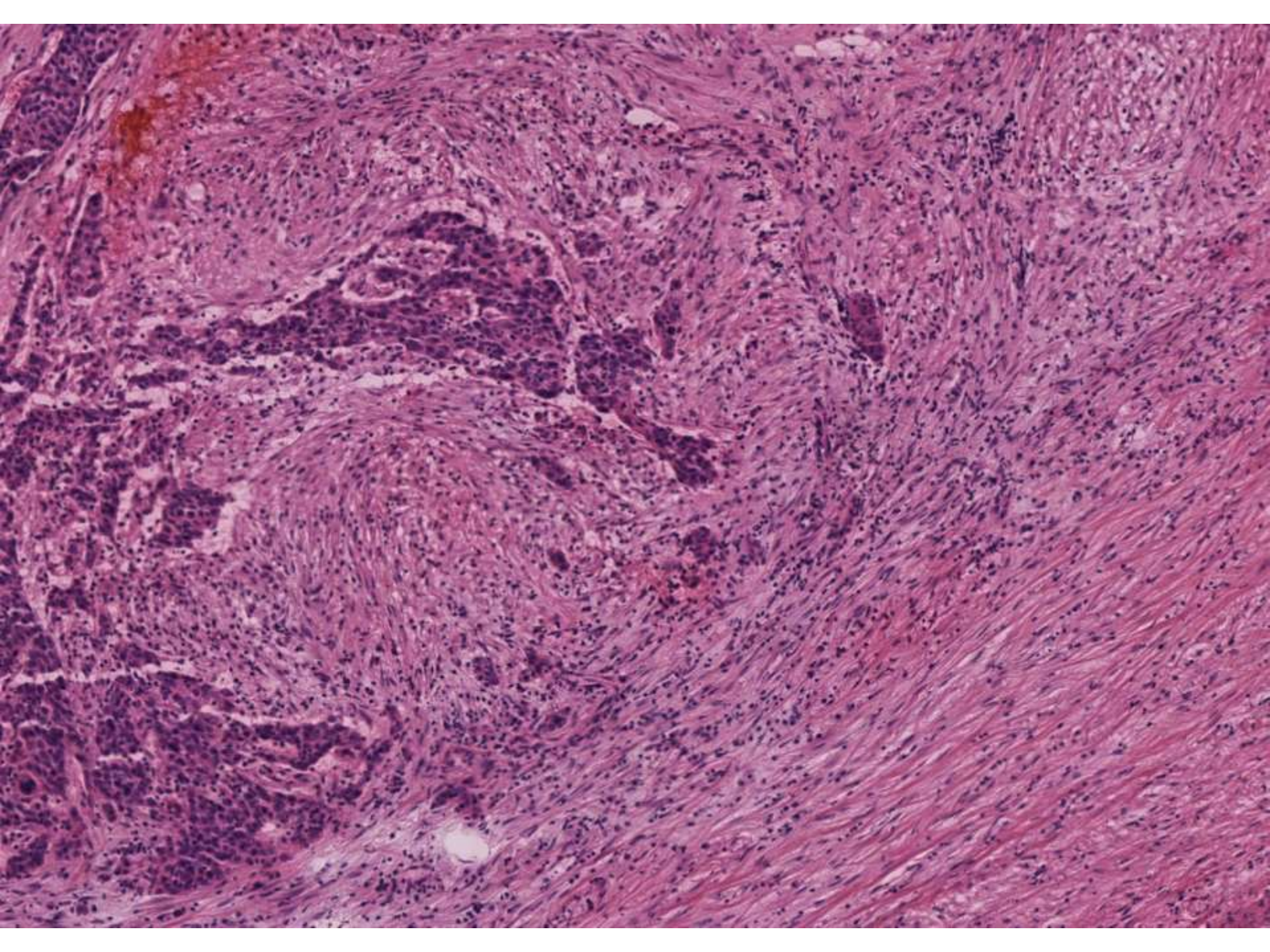
65-year-old male presenting for radical prostatectomy for prostate cancer (reportedly Gleason grade 4+5 disease with enlarged pelvic lymph nodes), by patient request (surgery was not recommended).

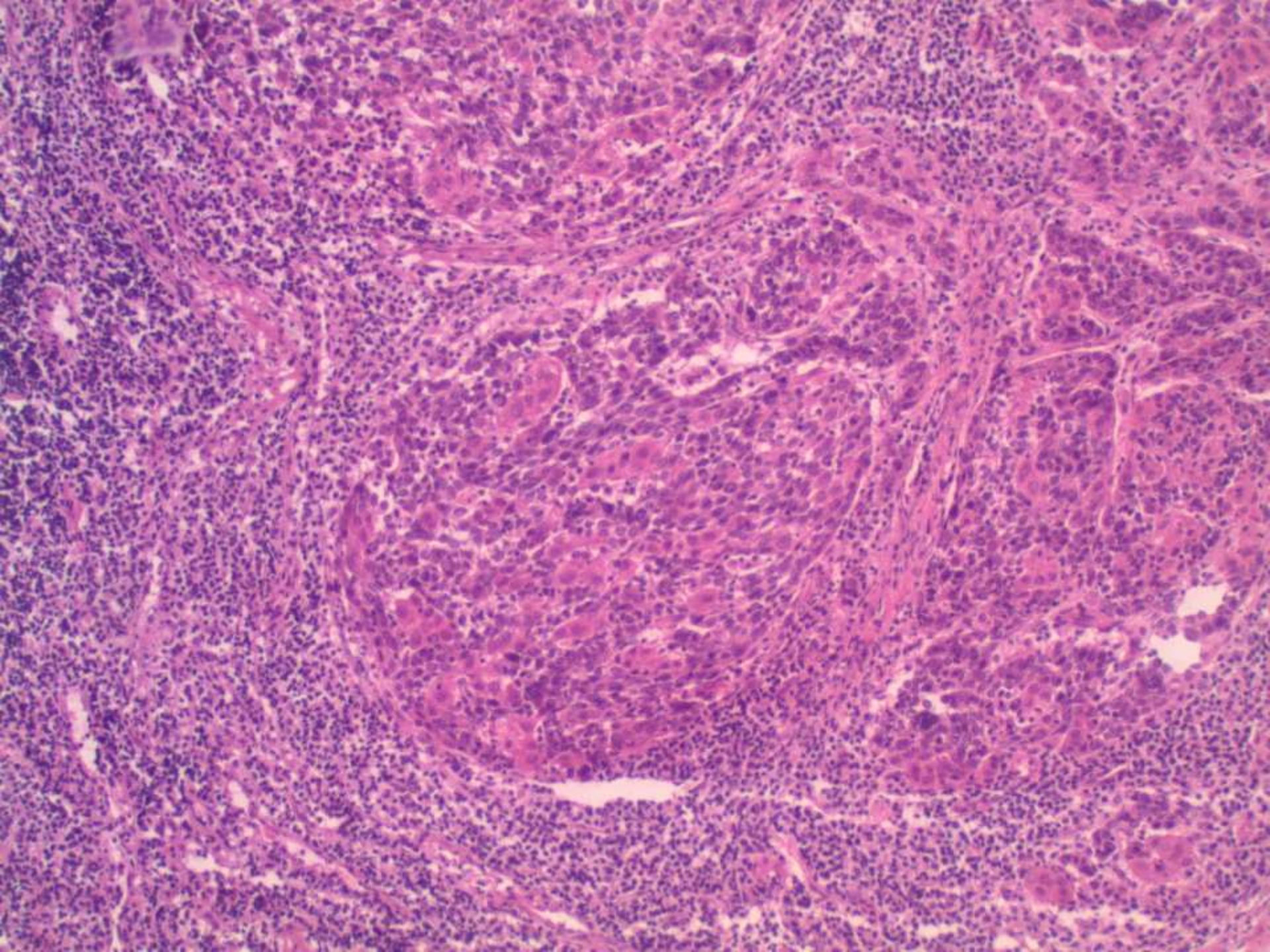
Patient had agreed that if intraoperative pelvic lymph nodes were positive by frozen section, surgery would be aborted. Frozen section slides of pelvic lymph node submitted.

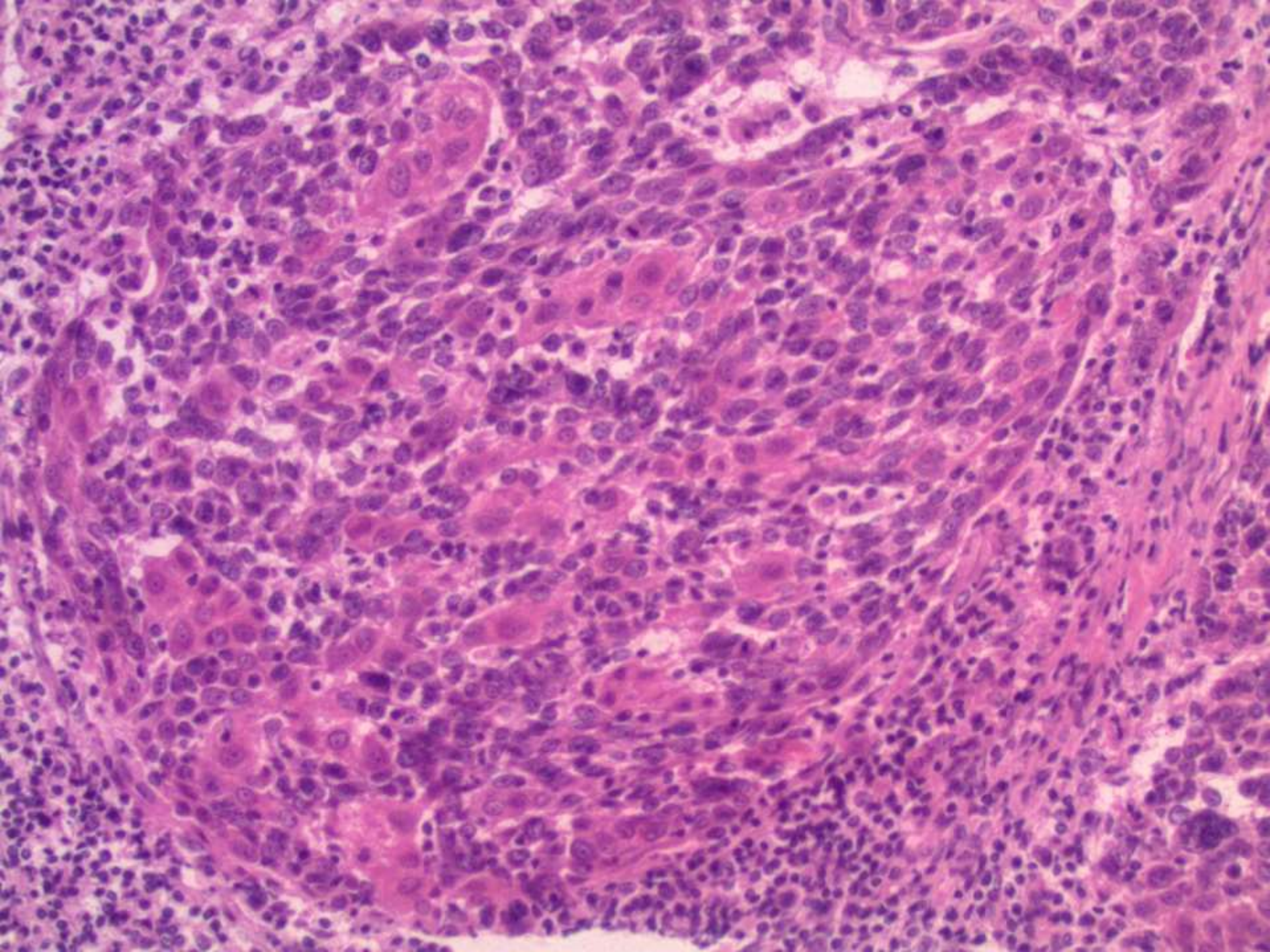


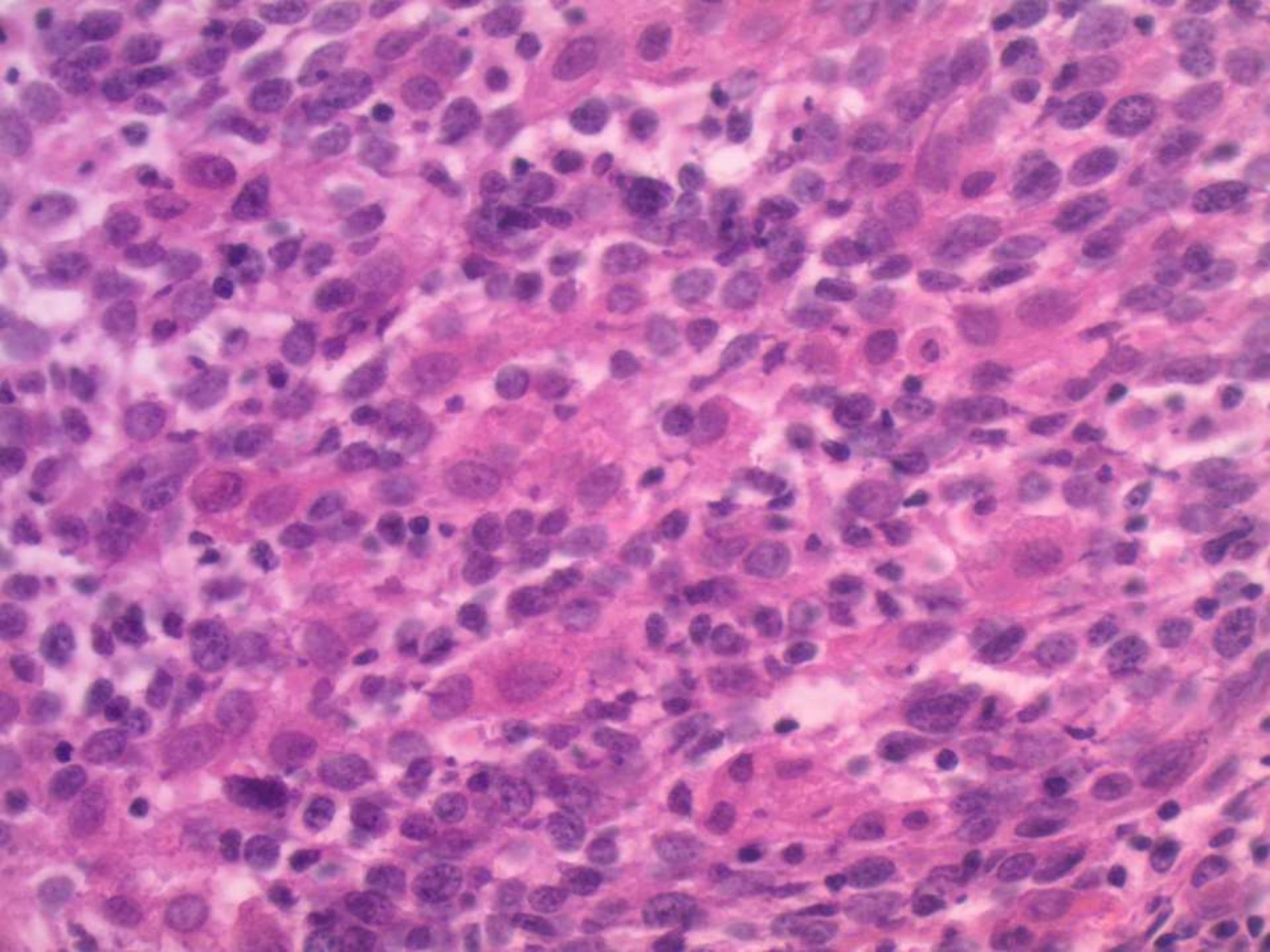


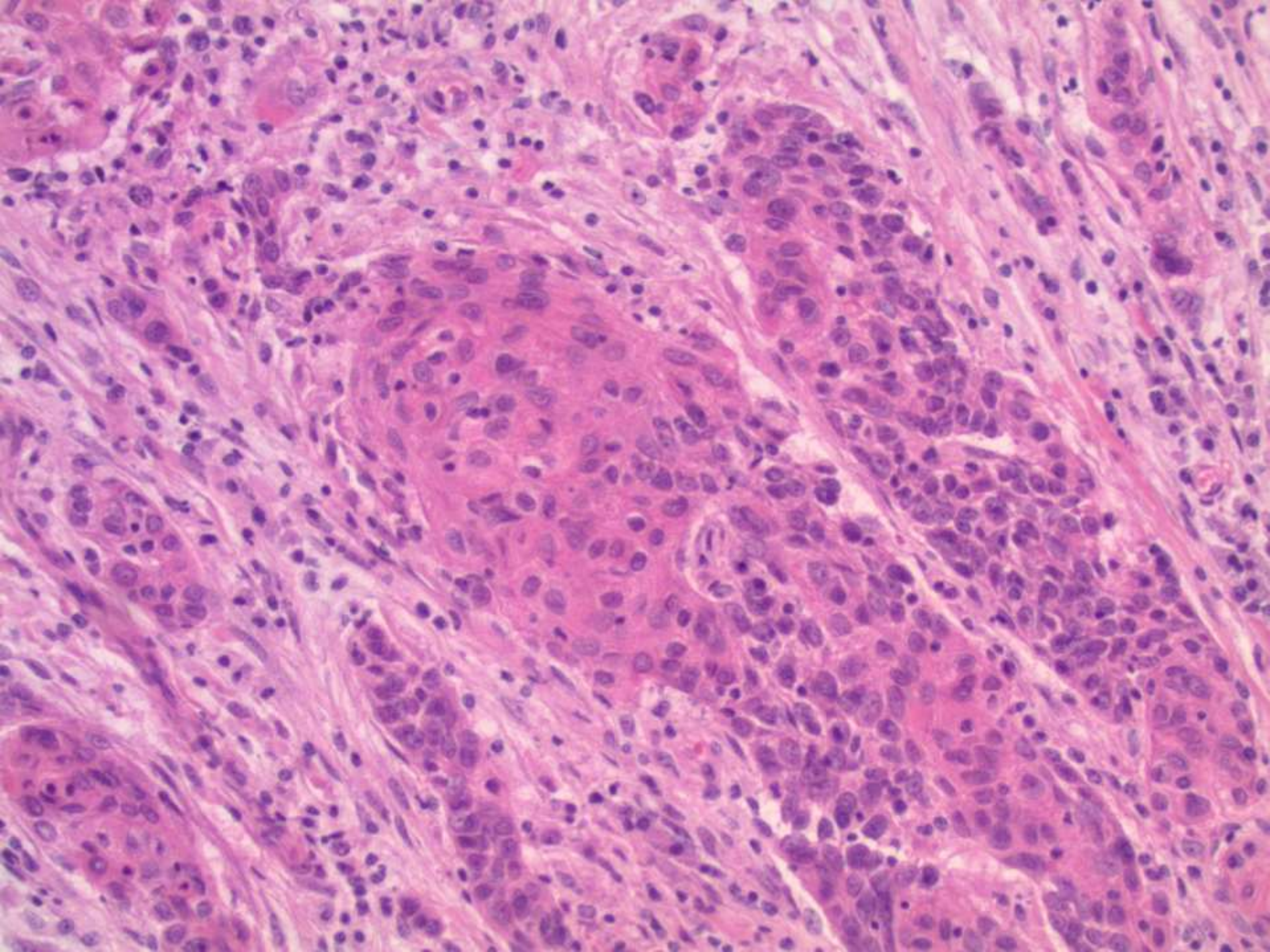


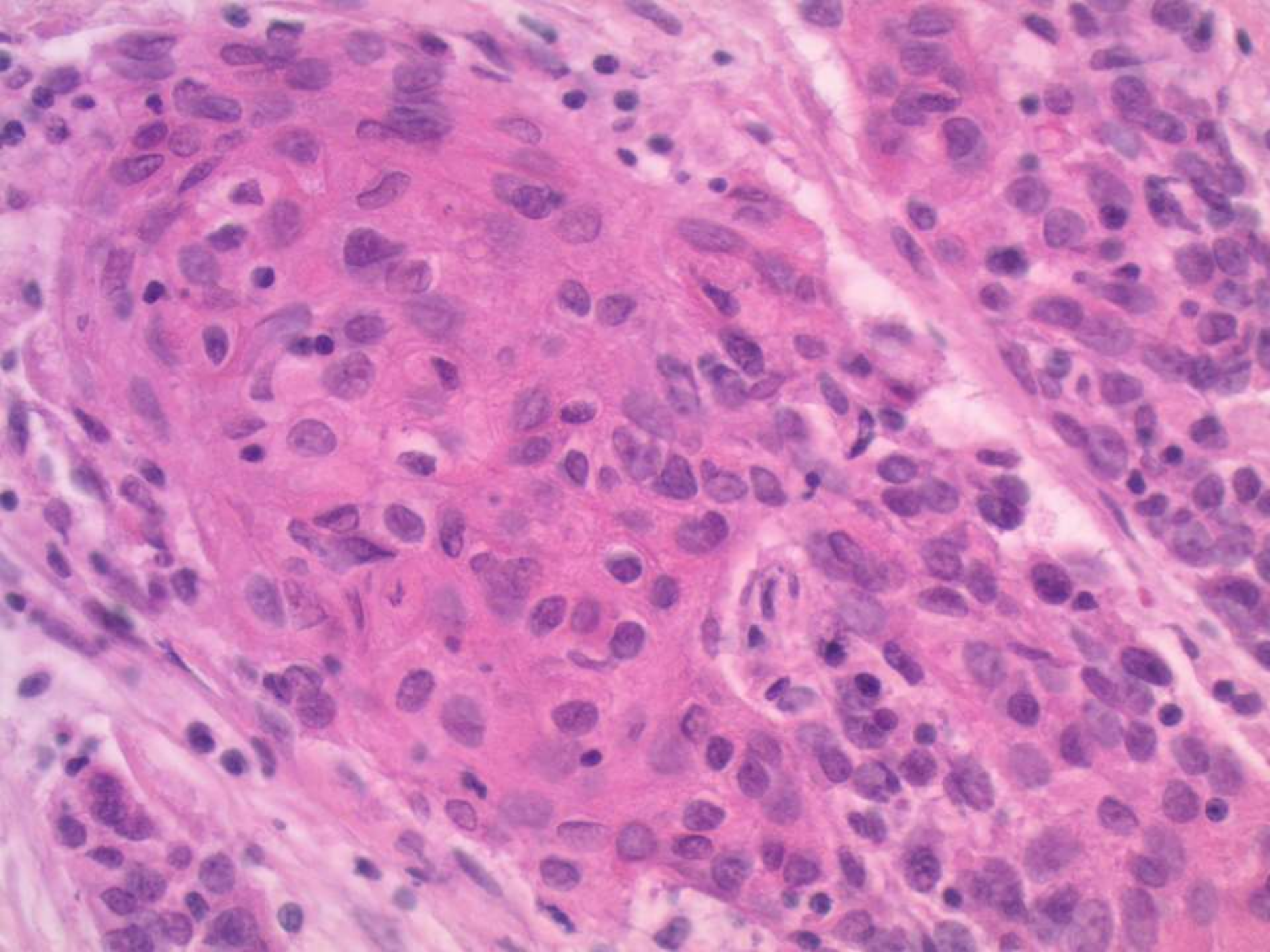


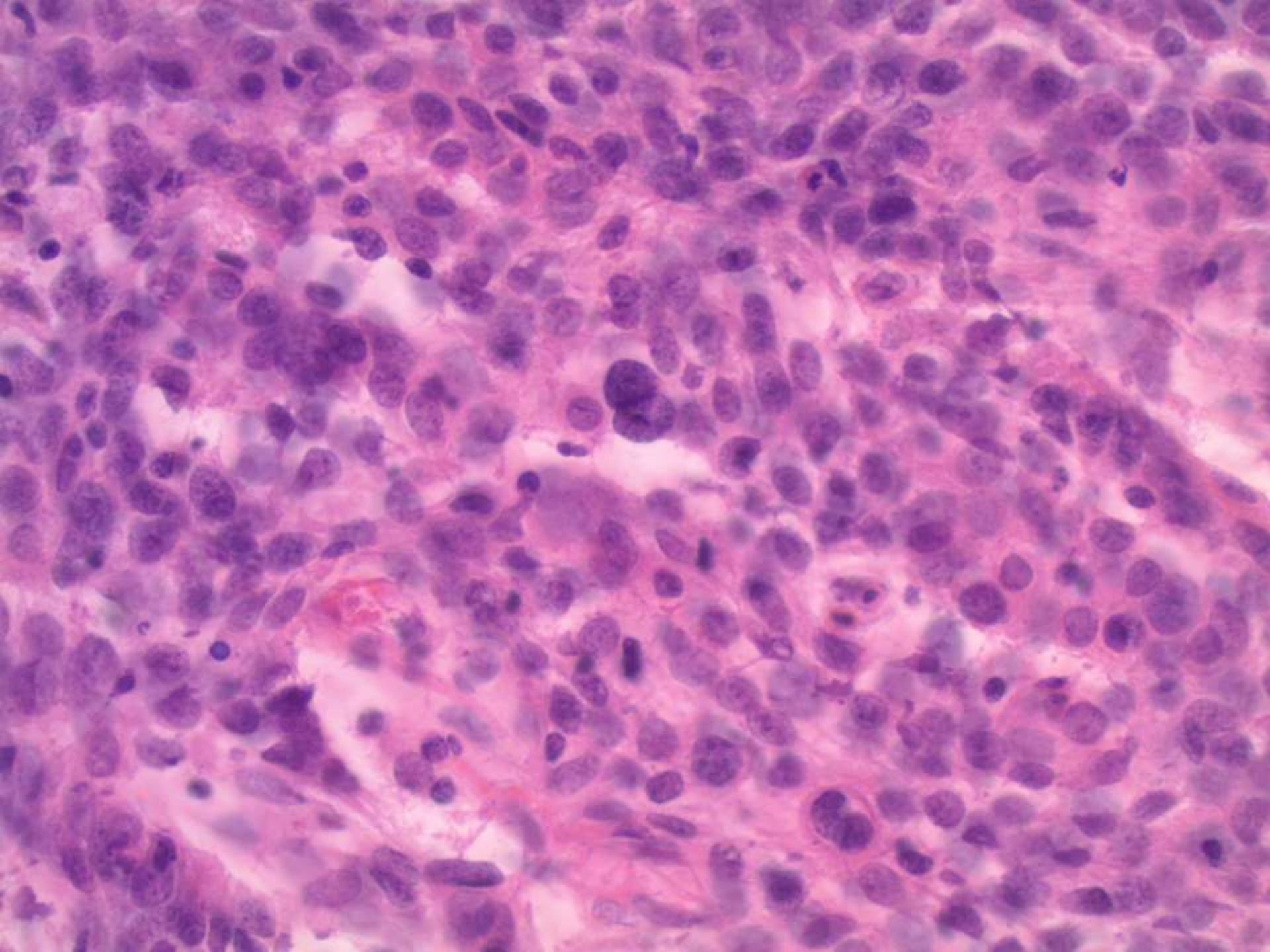




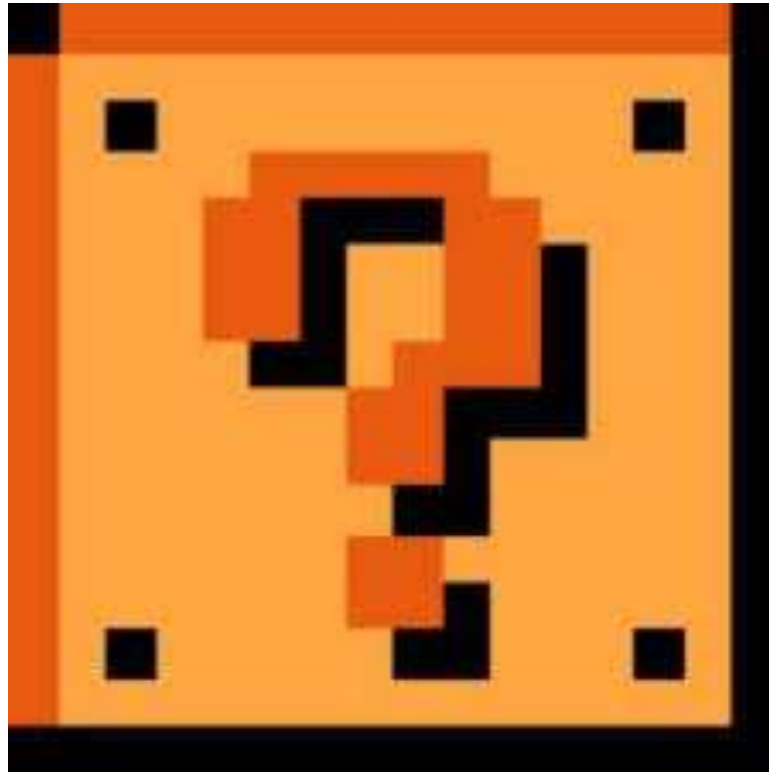


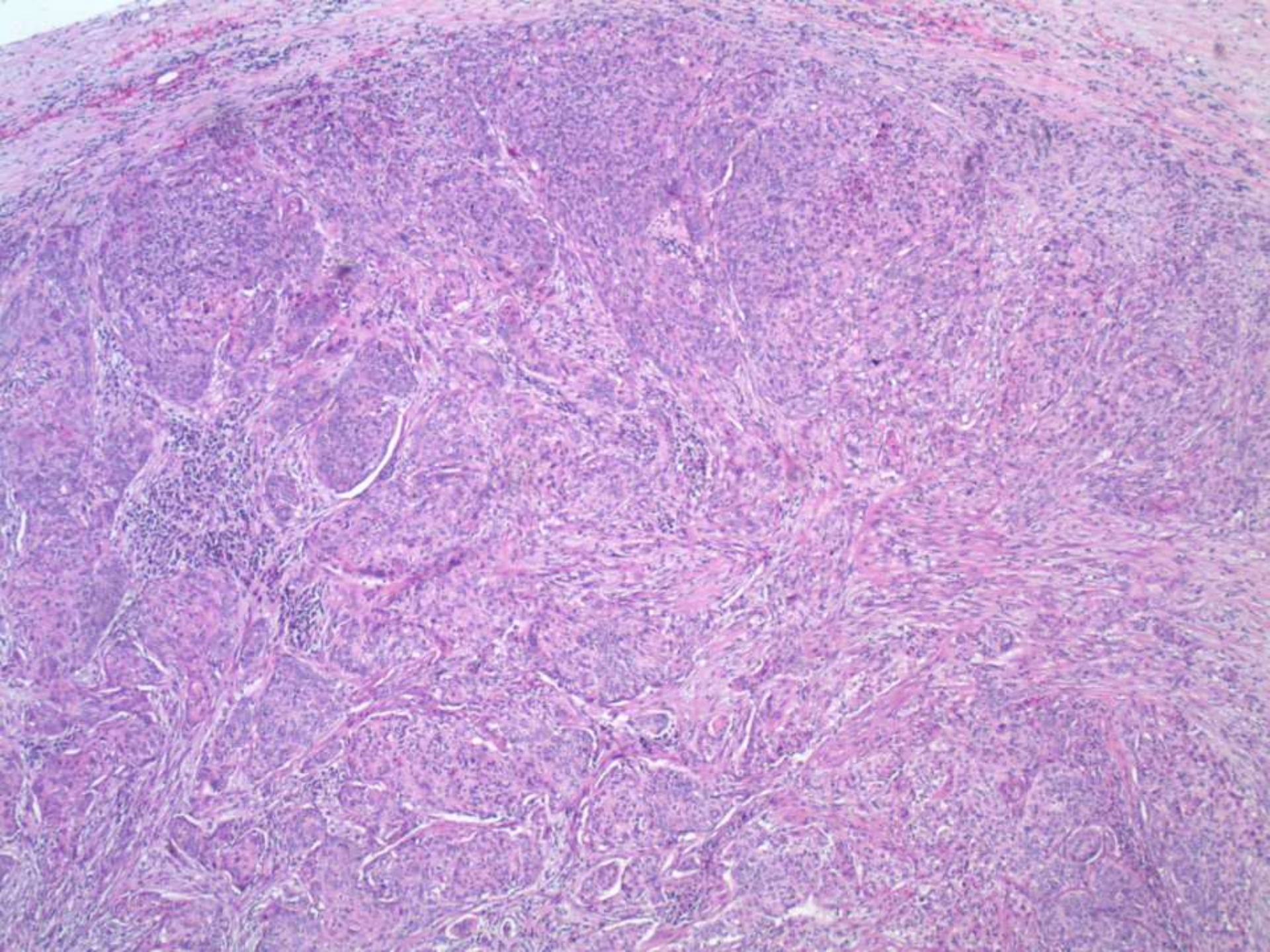


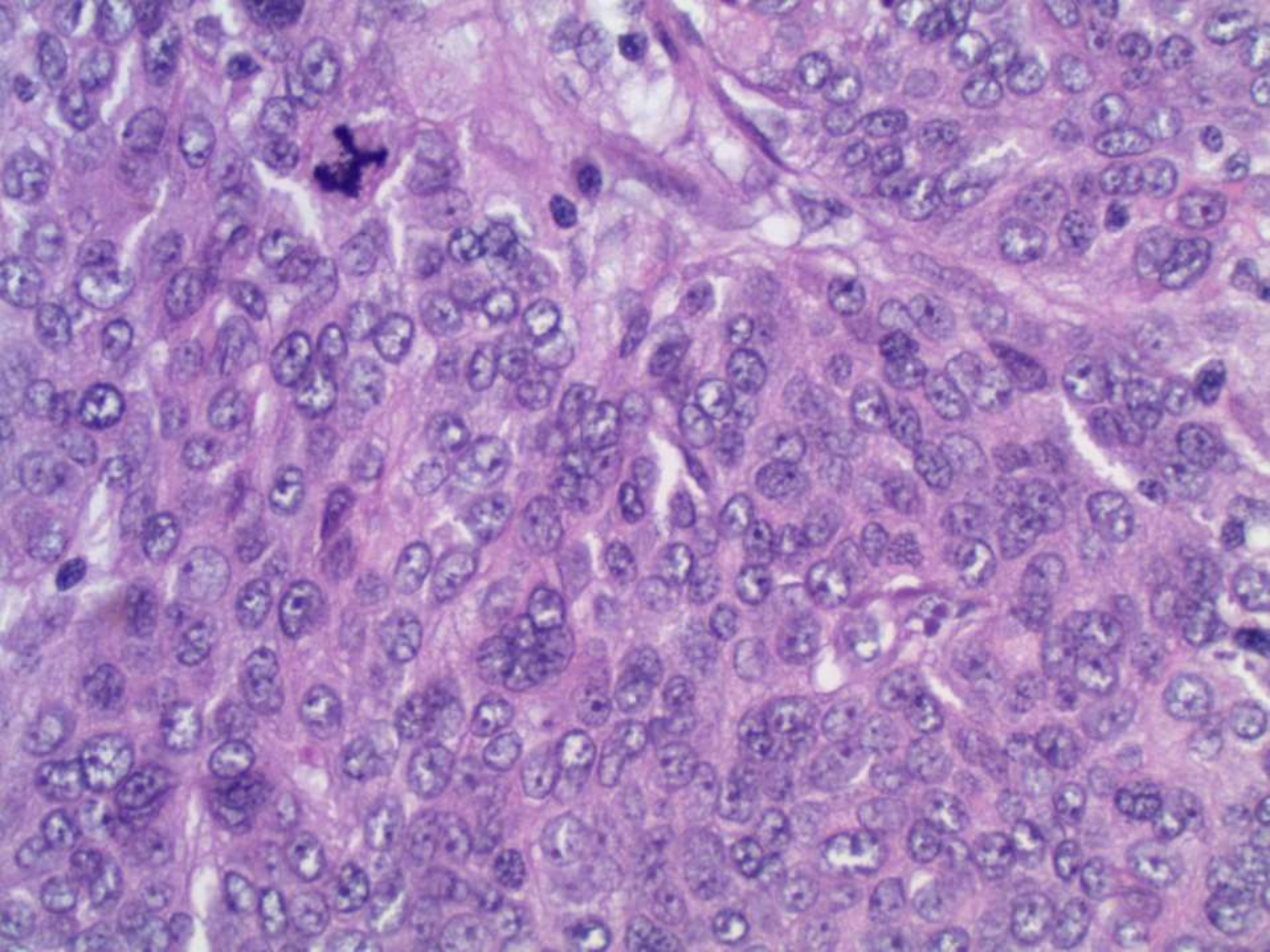


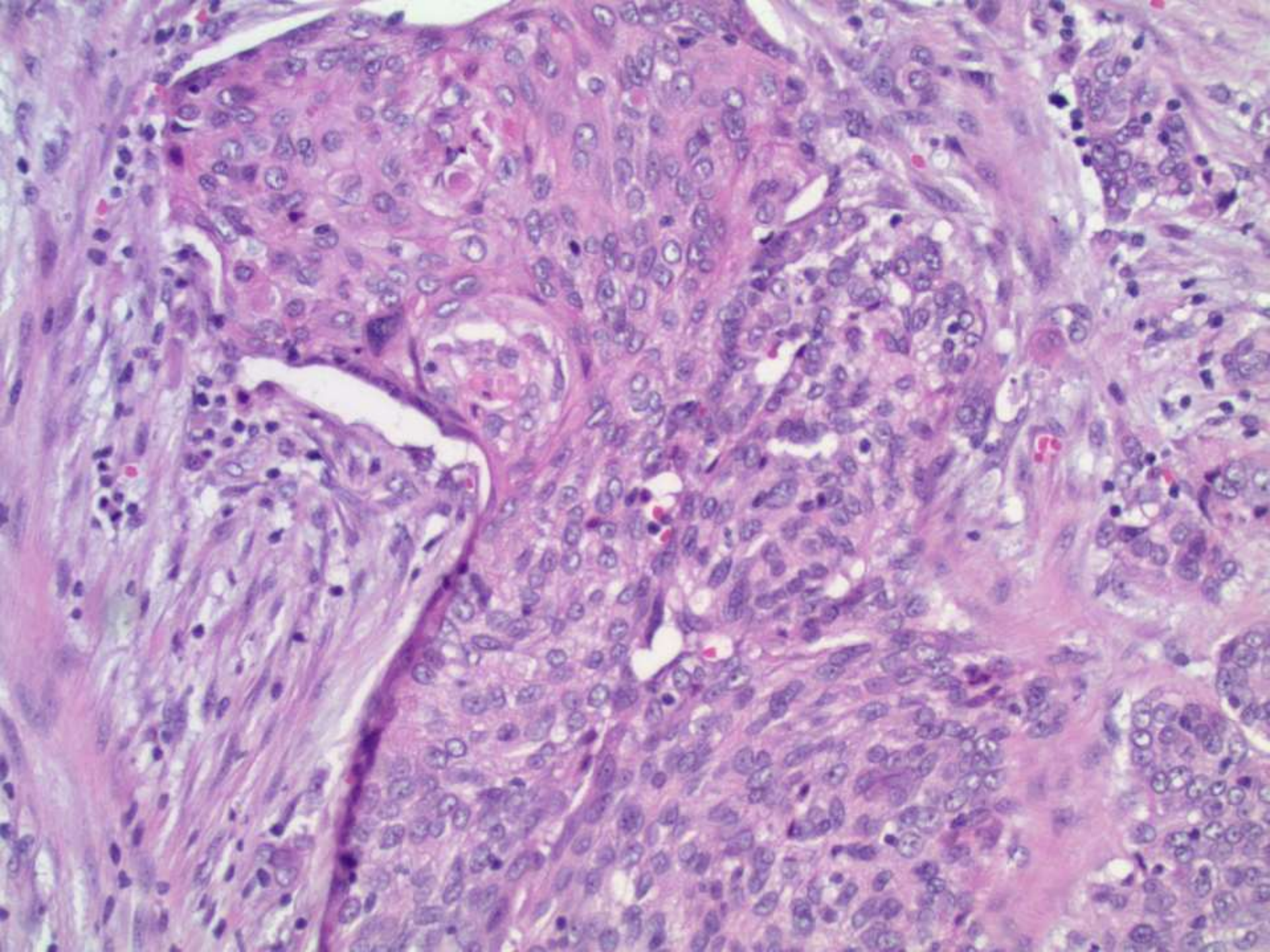


DIAGNOSIS?

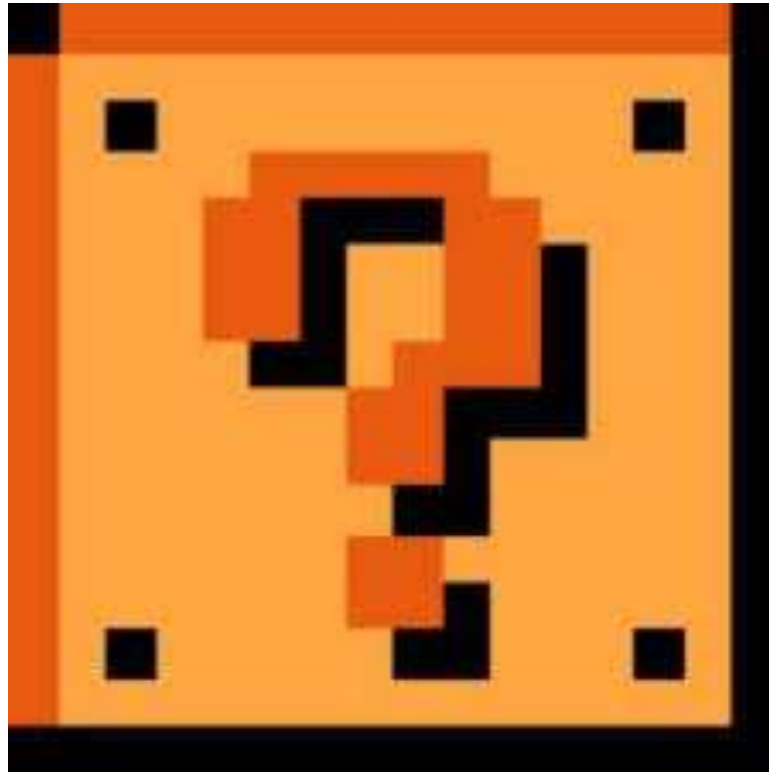








DIAGNOSIS?



A microscopic image of a tissue section, likely stained with hematoxylin and eosin (H&E). The image shows a dense population of cells with prominent, dark blue nuclei. The nuclei are mostly round or oval in shape. The background is a light, pinkish-white color, representing the cytoplasm and extracellular matrix. The text "NKX3.1/PSAP" is overlaid in the center in a bold, red font with a white outline.

NKX3.1/PSAP

A microscopic view of prostate tissue, showing numerous glandular structures lined by epithelial cells. The glands are closely packed and the cells have a characteristic appearance. The text "PSA" is overlaid in the center.

PSA



A high-magnification histological section of tissue, likely from a squamous epithelium, stained with hematoxylin and eosin (H&E). The tissue shows a dense population of cells with prominent, dark brown nuclei, characteristic of p63 staining. The cytoplasm and extracellular matrix are stained pink. The overall architecture suggests a neoplastic process, possibly a squamous cell carcinoma, given the strong p63 and CK5 staining. The text "p63/CK5" is overlaid in the center of the image.

p63/CK5

A microscopic image of a tissue section, likely a histological slide, showing numerous cells with blue-stained nuclei. The text "GATA3" is overlaid in the center in a bold, red, sans-serif font with a white outline and a slight drop shadow. The background is a light, off-white color with a dense distribution of small, dark blue spots representing the stained nuclei of the cells.

GATA3

A high-magnification light micrograph of a tissue section, likely from the urinary tract, showing numerous cells with prominent, dark blue nuclei. The cells are densely packed, and the overall appearance is characteristic of a histological stain like hematoxylin and eosin (H&E). The text 'uroplakin2' is overlaid in the center in a bold, red, sans-serif font with a slight drop shadow.

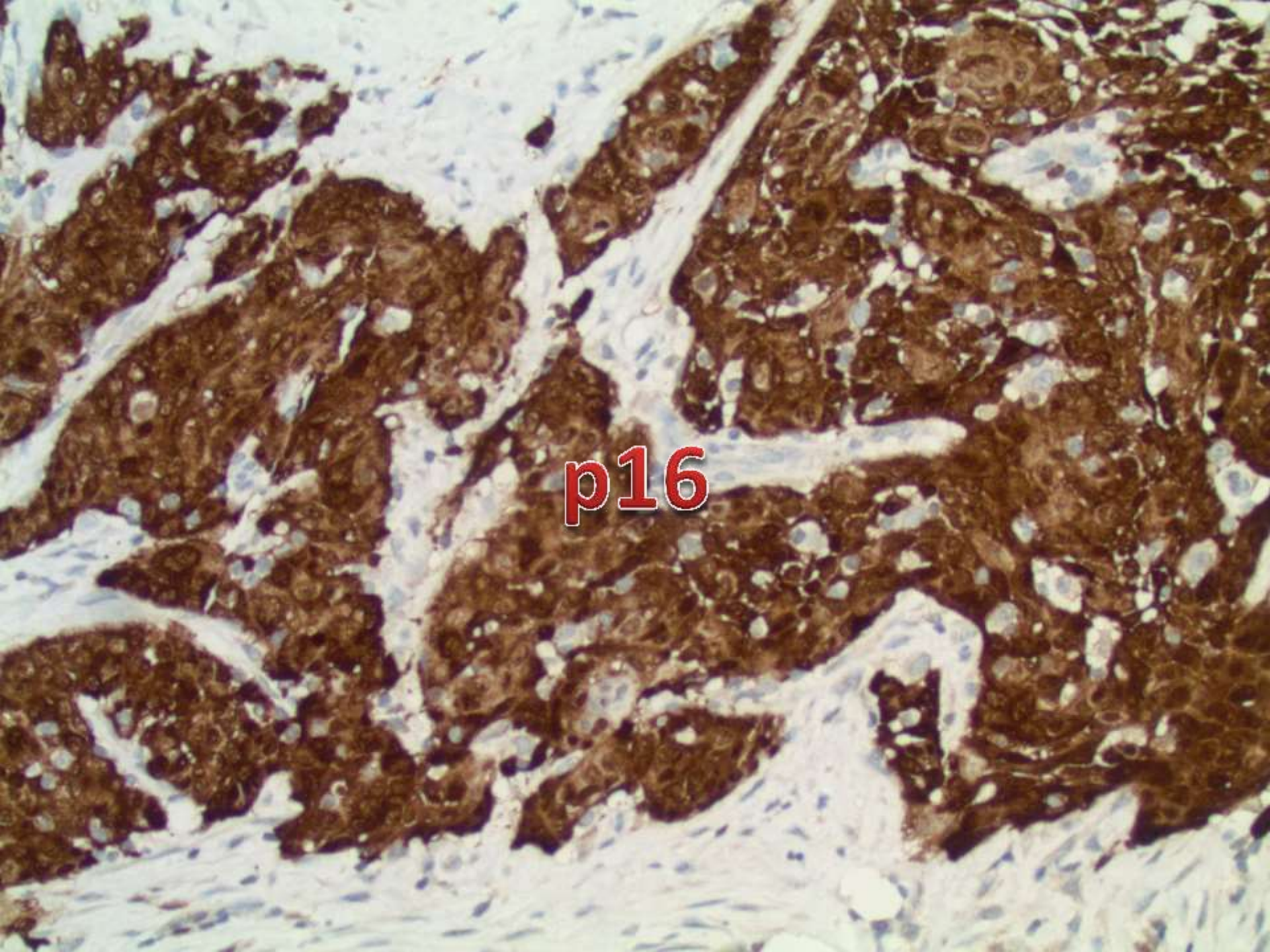
uroplakin2

A microscopic image of a tissue section, likely a histological slide, showing numerous cells with blue-stained nuclei. The cells are densely packed and exhibit varying degrees of nuclear atypia. The background is a light, pale yellowish-tan color. The text "CK7" is overlaid in the center in a bold, red, sans-serif font.

CK7



CK20



p16

HPV by ISH

HPV (FAMILY 6) ISH IS NEGATIVE FOR TYPES 6 AND 11.

HPV (FAMILY 16) ISH IS POSITIVE. THIS INDICATED POSITIVITY FOR ONE OR MORE OF THE FOLLOWING TYPES: 16, 18, 31, 33 OR 51.

DIAGNOSIS

- Lymph nodes, right & left pelvic, dissection:
 - Metastatic poorly differentiated carcinoma
 - p16 positive
 - Possible, but unusual pattern of spread for metastasis from tonsillar primary
 - Exclude other HPV-associated carcinomas
 - e.g. anorectal, penile carcinomas

FOLLOW-UP

(by report)

- Rectum nodules, biopsy:
 - Poorly differentiated carcinoma
 - Consistent with basaloid squamous cell carcinoma
 - p16/p63/CK5 positive